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=> d his

     (FILE 'HOME' ENTERED AT 12:23:26 ON 03 JUN 2002)

     FILE 'REGISTRY' ENTERED AT 12:24:19 ON 03 JUN 2002
L1             1 S 9004-54-0 ← CMD
L2           921 S 9004-54-0/CRN ← all mixtures (registered) comprising CMD
L3             1 S 79-14-1 ← HO-CH2-C(=O)-OH
L4          1936 S 79-14-1/CRN ← mixtures containing
L5            70 S L2 AND L4
L6        509625 S OC5/ES ← any pyran
L7             4 S L6 AND L5
L8        216531 S PETH/PCT ← any polymer w/ a poly ether
L9          2775 S L6 AND L8
L10         1216 S L9 AND "2-ETHANEDIYL" cpds w/ -CH2-CH2-O- frag
L11            0 S L2 AND L10
L12           27 S L2 AND L8
L13            0 S L9 AND L2
L14            2 S L4 AND L12
L15            1 S  195214-71-2

     FILE 'HCAPLUS' ENTERED AT 12:34:33 ON 03 JUN 2002
L16          435 S L5
L17       470851 S GLUCOSE OR GALACTOSE OR HEXOSE OR ?SACCHARIDE
L18           14 S L16(L)L17
L19       304673 S POLYETHYLEN? OR PEG OR ?ETHANEDIYL?
L20        13059 S LINKER
L21          262 S L19(L)L20
L22            0 S L21 AND L18
L23            1 S L18 AND L19
L24            1 S L18 AND L20
L25            2 S L23-24
L26           98 S L16 AND L17
L27           10 S L26 AND L19
L28            3 S L26 AND L20
L29           13 S L26 AND L27-28
L30           10 S L29 NOT L28
L31         7249 S L17(L)?CONJUGAT?
L32           29 S L31 AND L16
L33            3 S L32 AND (L19 OR L20)
L34         1042 S ?CARBOXYMETHYL(2W)DEXTRAN? OR CMD
L35         1099 S ?CARBOXYMETHYL?(2W)?DEXTRAN? OR CMD
L36           57 S L35 NOT L34
L37           71 S L34(L)CONJUGAT?
L38           18 S L31 AND L37
L39            3 S L28 AND L19-20
L40           18 S L38 NOT L39
L41           22 S L39-40 OR L33 OR L28 OR L25
                 SELECT RN L41 1-22

     FILE 'REGISTRY' ENTERED AT 12:55:07 ON 03 JUN 2002
L42          200 S E1-200
L43           46 S E201-246
L44          246 S L42-43
L45           28 S L44 AND   L1-15
L46          218 S L44 NOT L45

     FILE 'HCAPLUS' ENTERED AT 12:58:28 ON 03 JUN 2002
L47           22 S L41 AND L44
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22 citations

=> d ibib abs hitstr 1-22

L47 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:148739 HCAPLUS
DOCUMENT NUMBER: 136:205403
TITLE: DDS compounds of drugs having hydroxy groups
INVENTOR(S): Ousu, Satoru; Oki, Hitoshi; Naito, Hiroyuki; Hirotani, Kenji
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002060351	A2	20020226	JP 2001-80188	20010321

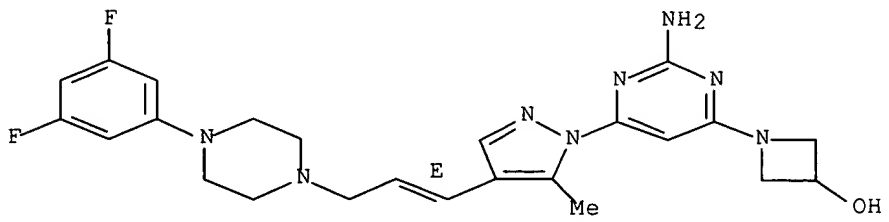
PRIORITY APPLN. INFO.: JP 2000-79655 A 20000322
OTHER SOURCE(S): MARPAT 136:205403

AB The DDS (drug delivery system) compds. are represented by the formula AWN(R1)C(R2)(R3)OQ or PZN(R1)C(R2)(R3)OQ [A = polymeric carrier for drugs; W = spacer contg. amino acid or oligopeptide residue linked to N at the C-terminal; P = protective group for H or NH2; Z = amino acid residue or oligopeptide residue linked to N at the C-terminal; R1-R3 = H, (substituted) alkyl, (substituted) aryl, carboxyl, alkoxycarbonyl; 2 of R1-R3 may form 4- to 8-membered ring; OQ = residue of OH-contg. drugs]. Tert-Bu 13-[[1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]-7-benzyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazatri-1-decylcarbamate (prepn. given) showed 89% release of 1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinol (I) in murine fibrosarcoma Meth-A cell homogenate at 40.degree. and pH 4.5 and <1% release of I in a buffer at pH 4.5. I.v. administration of a carboxymethyl dextran polyol deriv. of I (linked through an oligopeptide and aminomethylene **linker**) at 10 mg/kg as I showed significant antitumor effect and did not cause diarrhea in mice.

IT **401470-57-3**
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. of amino acid or peptide derivs. of hydroxy-contg. drugs for DDS)

RN 401470-57-3 HCAPLUS
CN 3-Azetidinol, 1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **39422-83-8DP**, Carboxymethyldextran sodium salt, polyols, conjugates with peptide spacers and antitumor drugs **401470-32-4P**
401470-34-6DP, conjugates with carboxymethyl dextran polyols
401470-36-8DP, conjugates with carboxymethyl dextran polyols
401470-38-0DP, conjugates with carboxymethyl dextran polyols
401470-40-4DP, conjugates with carboxymethyl dextran polyols
401470-44-8DP, conjugates with carboxymethyl dextran polyols
401470-48-2DP, conjugates with carboxymethyl dextran polyols
401470-52-8DP, conjugates with carboxymethyl dextran polyols
401470-56-2DP, conjugates with carboxymethyl dextran polyols
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid or peptide derivs. of hydroxy-contg. drugs for DDS)

RN 39422-83-8 HCAPLUS
CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

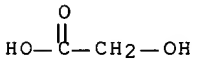
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

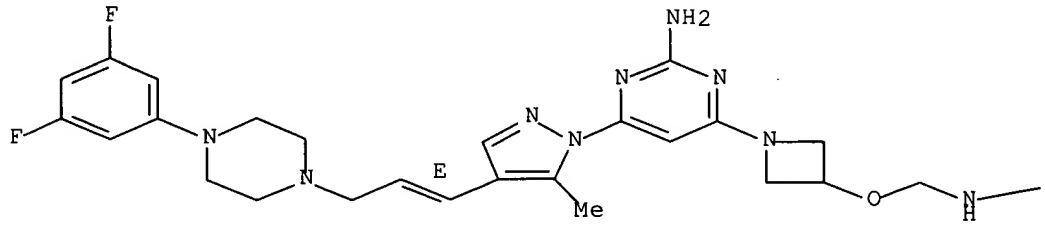
CRN 79-14-1
CMF C2 H4 O3



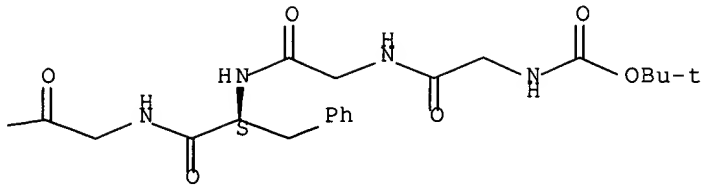
RN 401470-32-4 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



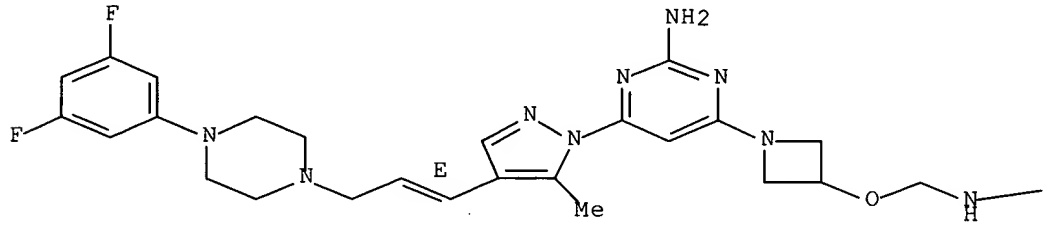
PAGE 1-B



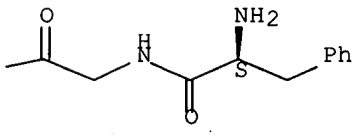
RN 401470-34-6 HCAPLUS
CN Glycinamide, L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



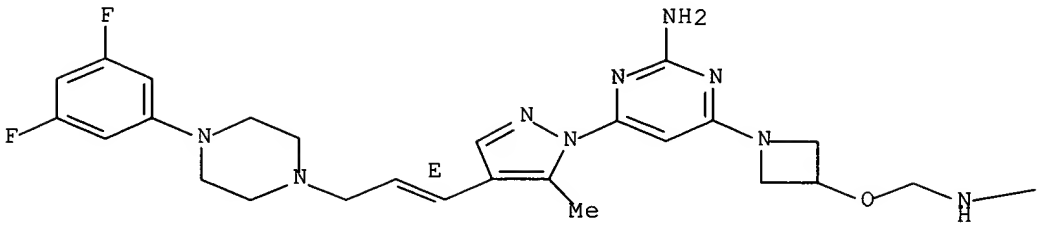
PAGE 1-B



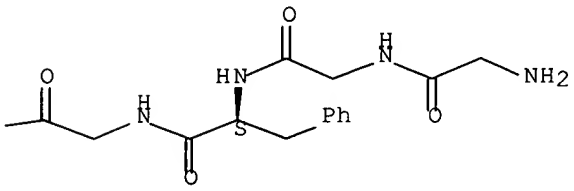
RN 401470-36-8 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



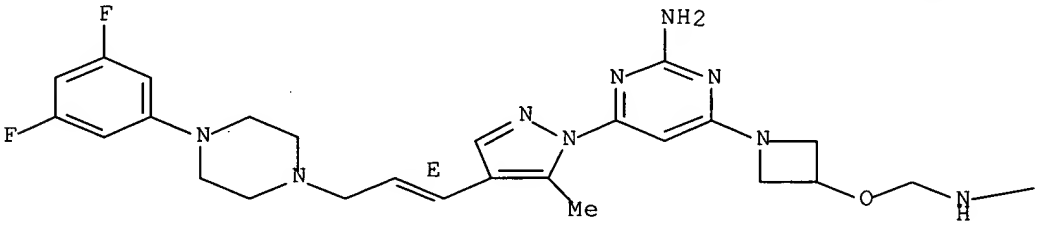
PAGE 1-B



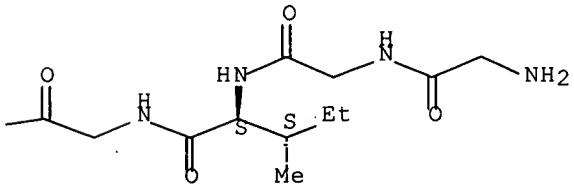
RN 401470-38-0 HCAPLUS
CN Glycinamide, glycylglycyl-L-isoleucyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



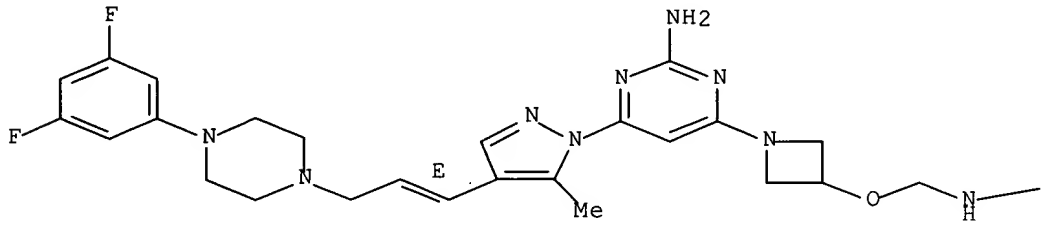
PAGE 1-B



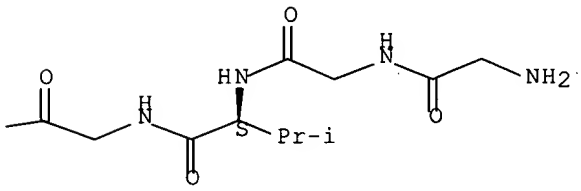
RN 401470-40-4 HCAPLUS
CN Glycinamide, glycylglycyl-L-valyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



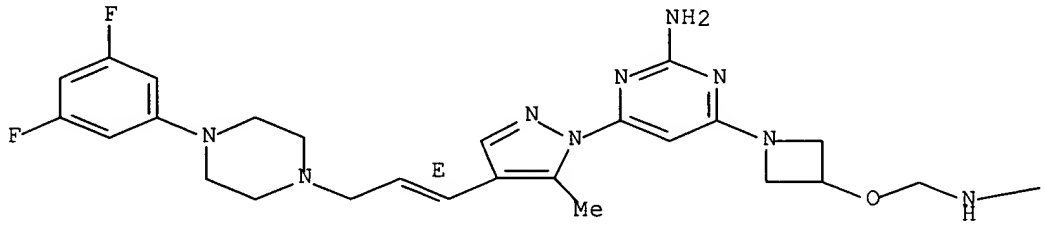
PAGE 1-B



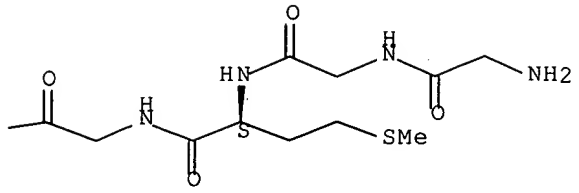
RN 401470-44-8 HCAPLUS
CN Glycinamide, glycylglycyl-L-methionyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



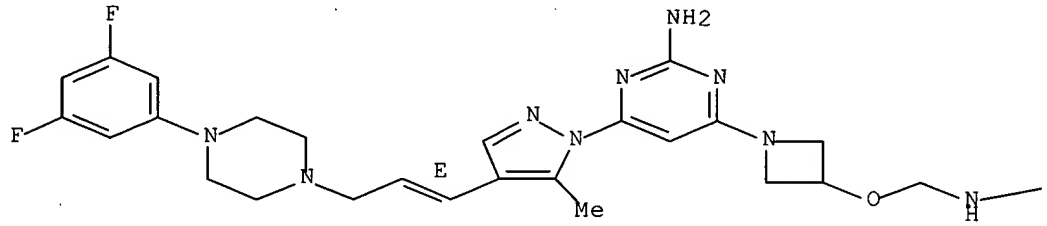
PAGE 1-B



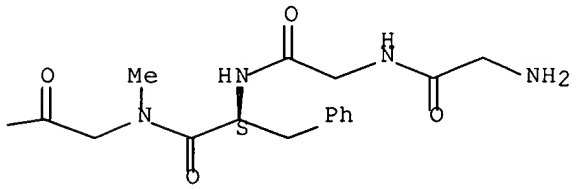
RN 401470-48-2 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



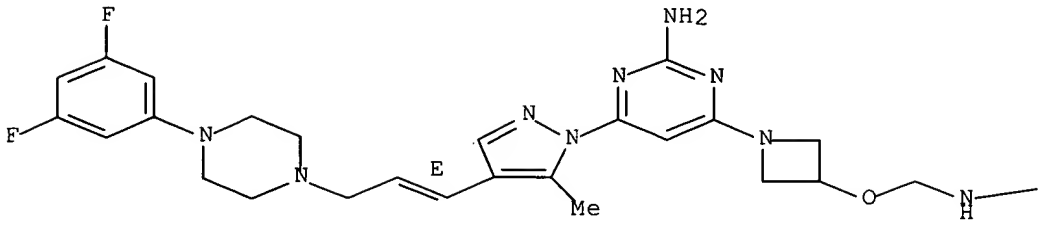
PAGE 1-B



RN 401470-52-8 HCAPLUS
CN L-Isoleucinamide, glycylglycyl-L-prolyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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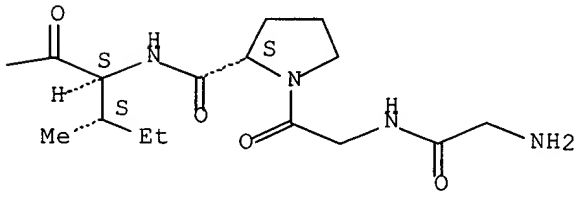
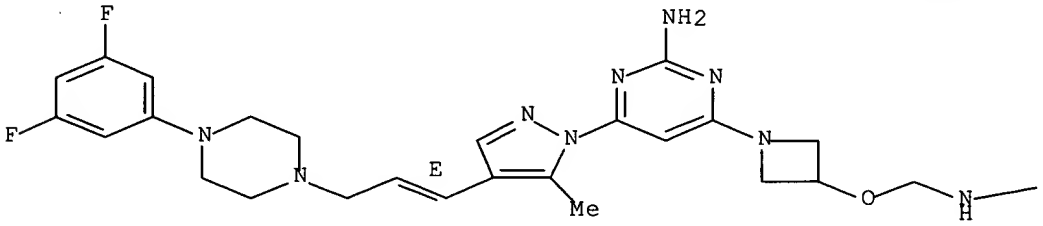
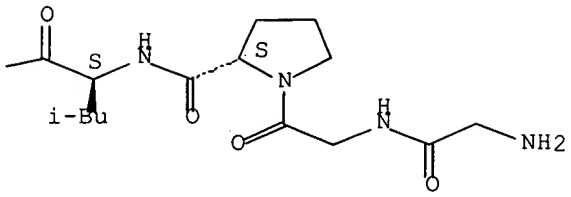


RN 401470-56-2 HCAPLUS
CN L-Leucinamide, glycylglycyl-L-prolyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

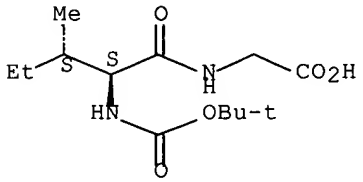
PAGE 1-A



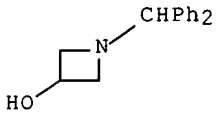


IT **16257-05-9 18621-17-5**, 1-Benzhydryl-3-azetidinol
31972-52-8 32991-17-6 35661-40-6
35665-38-4 39621-73-3 71989-28-1
160036-44-2 256930-32-2 333366-34-0
401470-59-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino acid or peptide derivs. of hydroxy-contg. drugs for DDS)
RN 16257-05-9 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-isoleucyl- (9CI) (CA INDEX NAME)

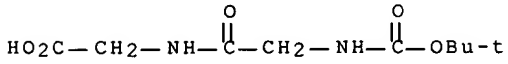
Absolute stereochemistry.



RN 18621-17-5 HCAPLUS
CN 3-Azetidinol, 1-(diphenylmethyl)- (8CI, 9CI) (CA INDEX NAME)

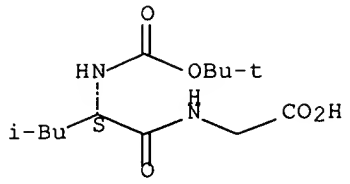


RN 31972-52-8 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycyl- (9CI) (CA INDEX NAME)



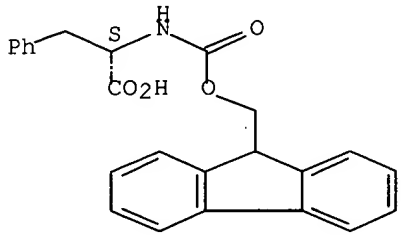
RN 32991-17-6 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

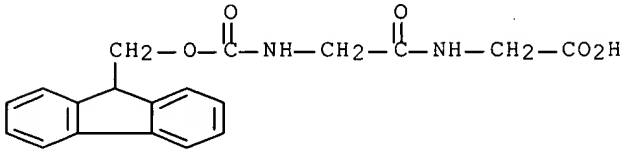


RN 35661-40-6 HCAPLUS
CN L-Phenylalanine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

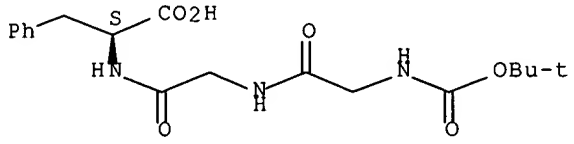


RN 35665-38-4 HCAPLUS
CN Glycine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycyl- (9CI) (CA INDEX NAME)



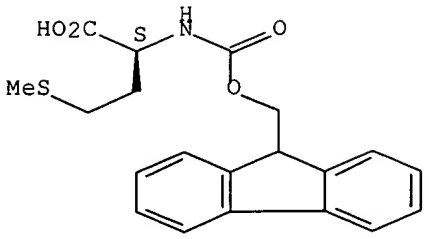
RN 39621-73-3 HCAPLUS
CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



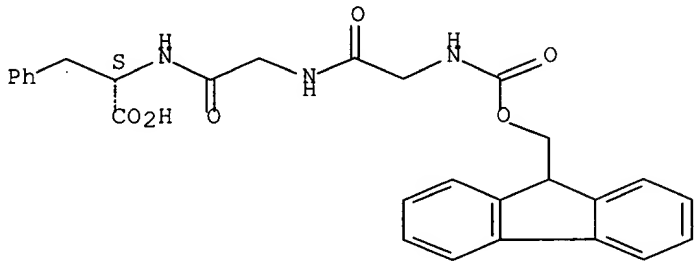
RN 71989-28-1 HCAPLUS
CN L-Methionine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



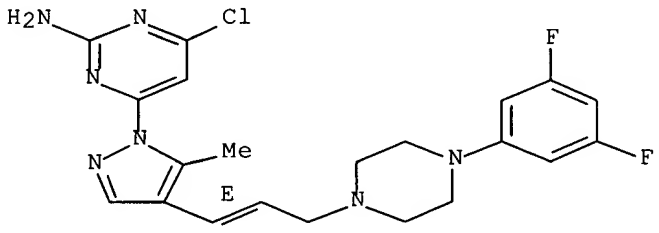
RN 160036-44-2 HCAPLUS
CN L-Phenylalanine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



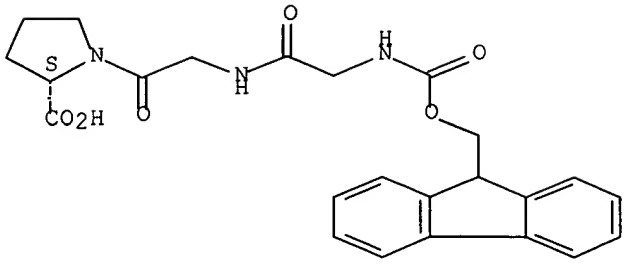
RN 256930-32-2 HCAPLUS
CN 2-Pyrimidinamine, 4-chloro-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



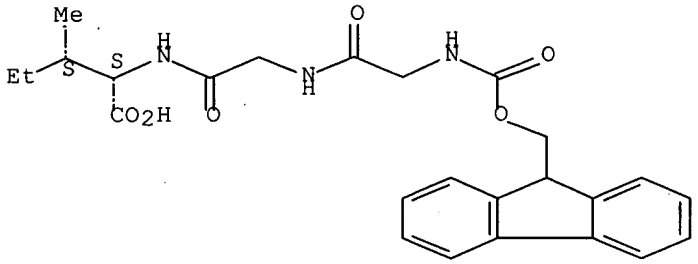
RN 333366-34-0 HCAPLUS
CN L-Proline, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



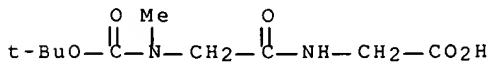
RN 401470-59-5 HCAPLUS
CN L-Isoleucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **60667-52-9P 401470-30-2P 401470-31-3P**
401470-33-5P 401470-34-6P 401470-35-7P
401470-36-8P 401470-37-9P 401470-38-0P
401470-39-1P 401470-40-4P 401470-41-5P
401470-42-6P 401470-43-7P 401470-44-8P
401470-45-9P 401470-46-0P 401470-47-1P
401470-48-2P 401470-49-3P 401470-50-6P
401470-51-7P 401470-52-8P 401470-53-9P
401470-54-0P 401470-55-1P 401470-56-2P
401470-58-4P 401470-60-8P 401470-61-9P
401470-62-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid or peptide derivs. of hydroxy-contg. drugs for DDS)

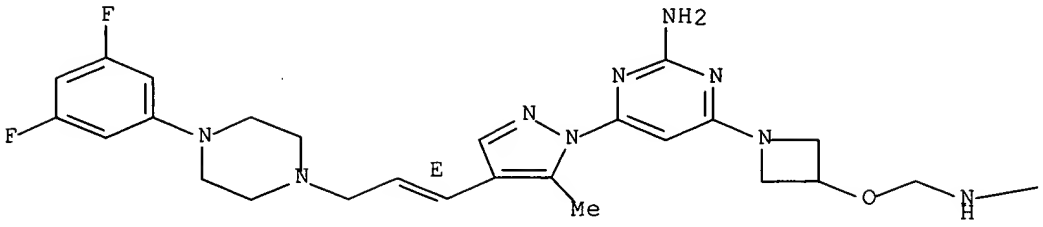
RN 60667-52-9 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-N-methylglycyl- (9CI) (CA INDEX NAME)



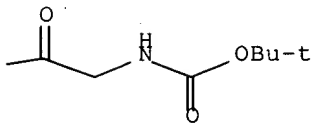
RN 401470-30-2 HCAPLUS
CN Carbamic acid, [2-[[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]amino]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

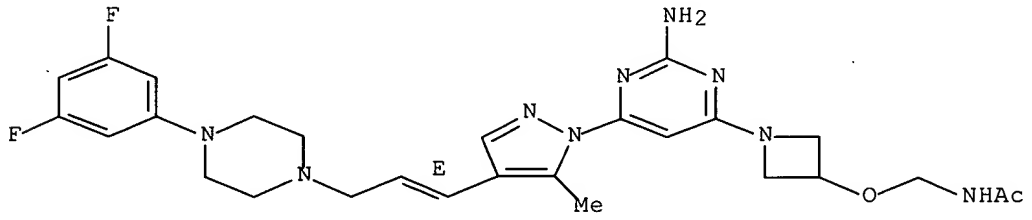


PAGE 1-B



RN 401470-31-3 HCAPLUS
CN Acetamide, N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

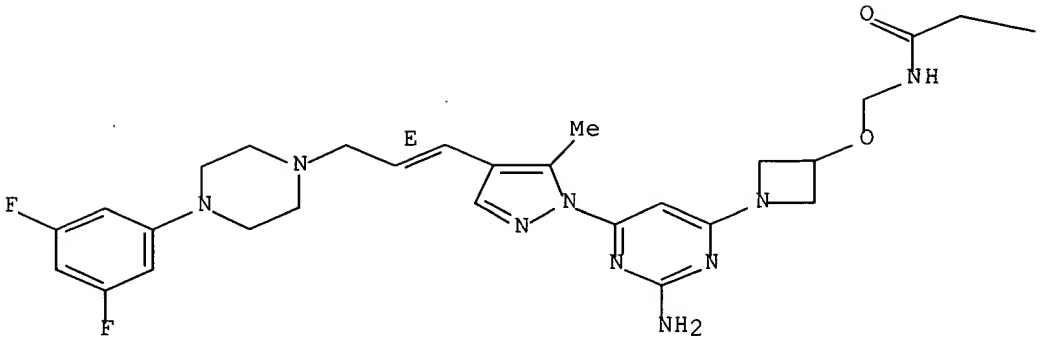
Double bond geometry as shown.



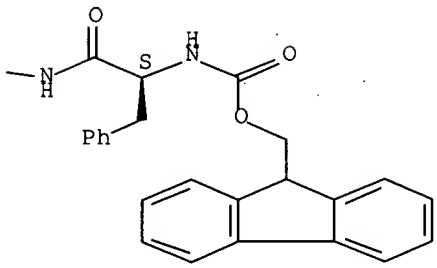
RN 401470-33-5 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



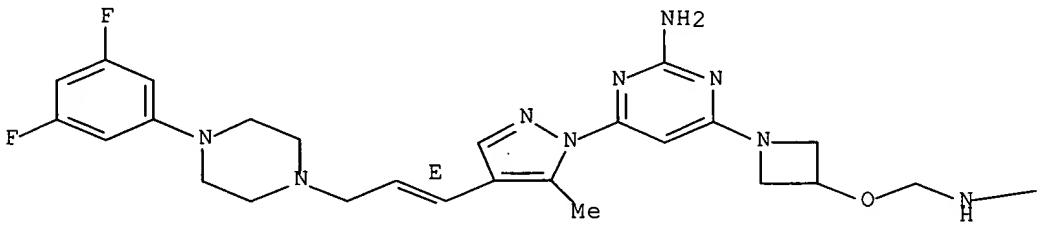
PAGE 1-B



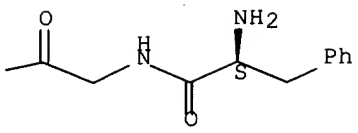
RN 401470-34-6 HCAPLUS
CN Glycinamide, L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



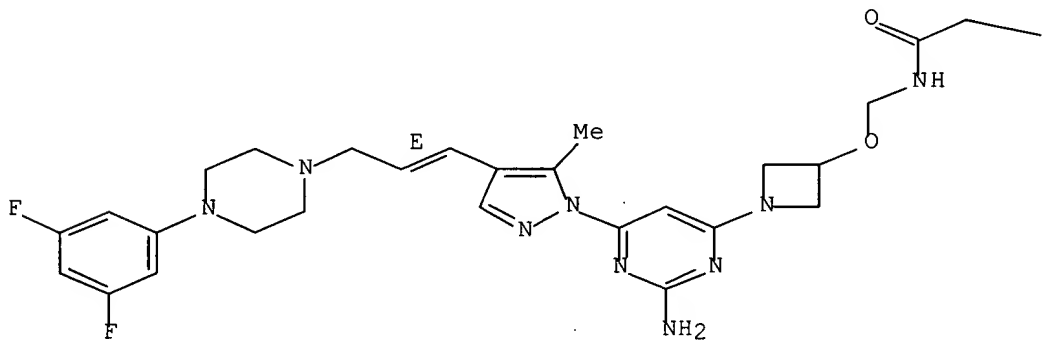
PAGE 1-B



RN 401470-35-7 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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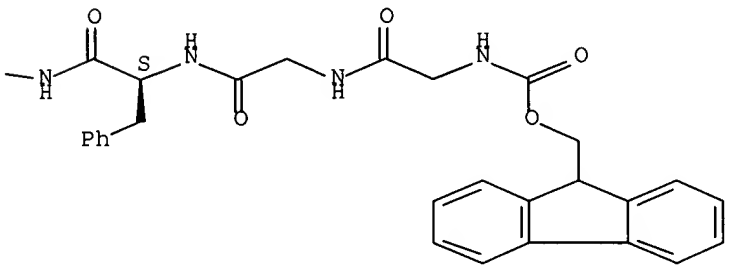
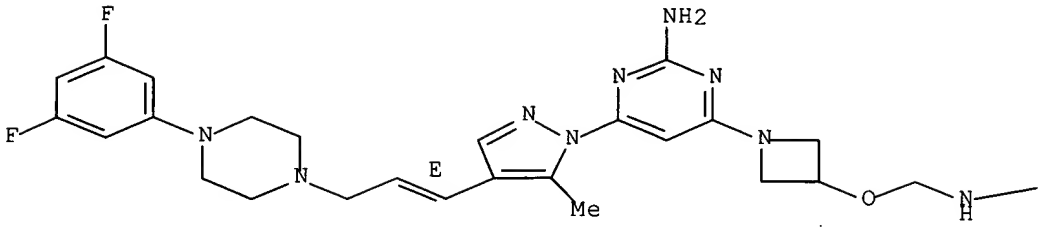


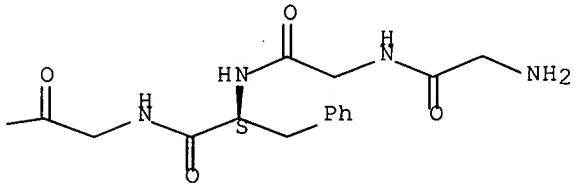
RN 401470-36-8 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



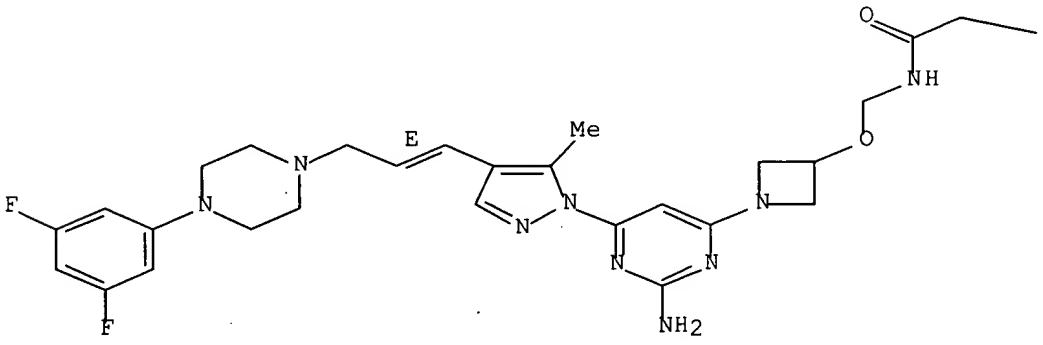
PAGE 1-B



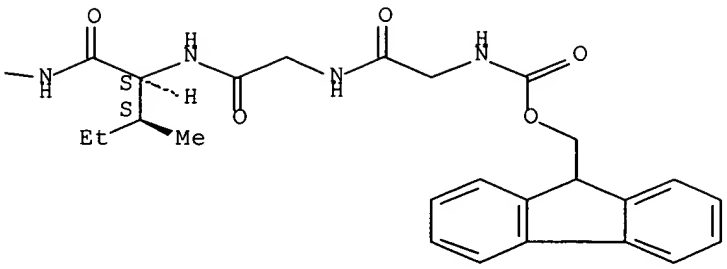
RN 401470-37-9 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-isoleucyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



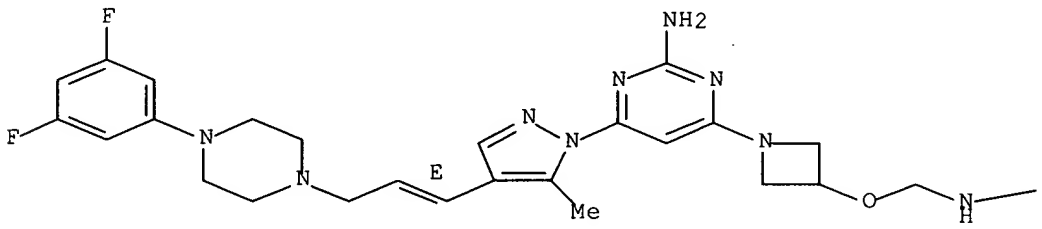
PAGE 1-B



RN 401470-38-0 HCAPLUS
CN Glycinamide, glycylglycyl-L-isoleucyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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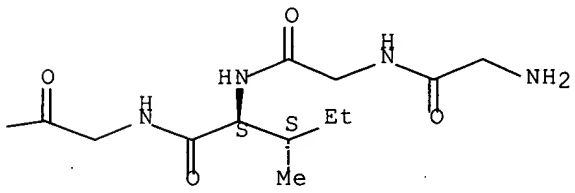
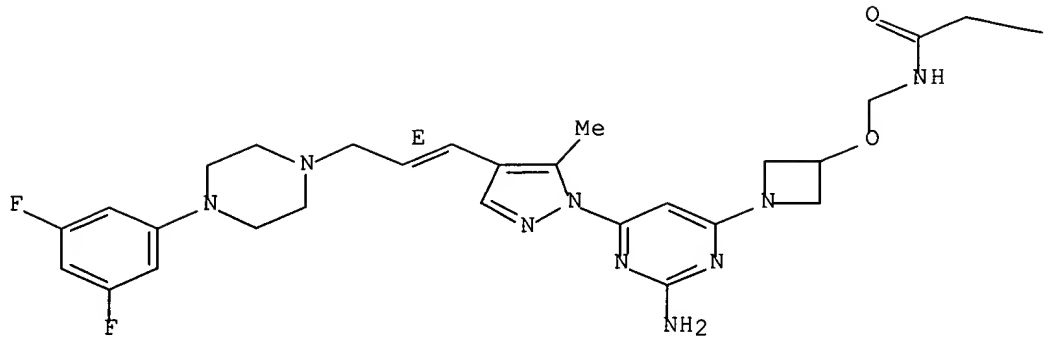


RN 401470-39-1 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-valyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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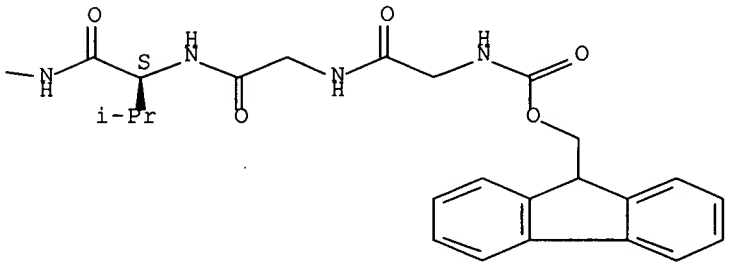
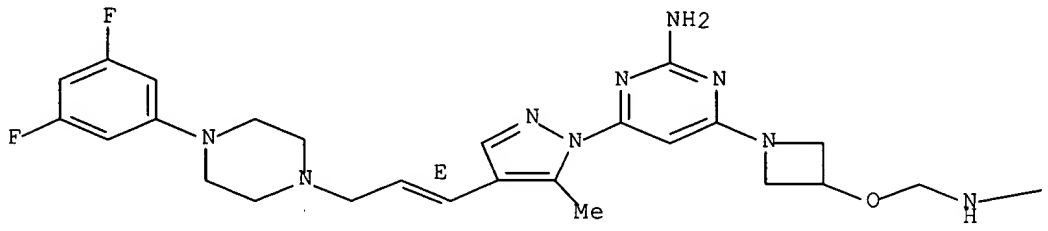


RN 401470-40-4 HCAPLUS
CN Glycinamide, glycylglycyl-L-valyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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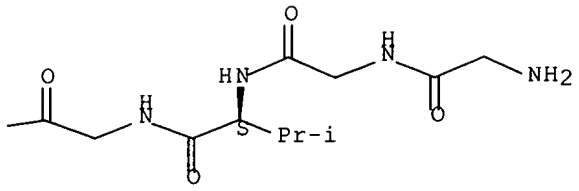
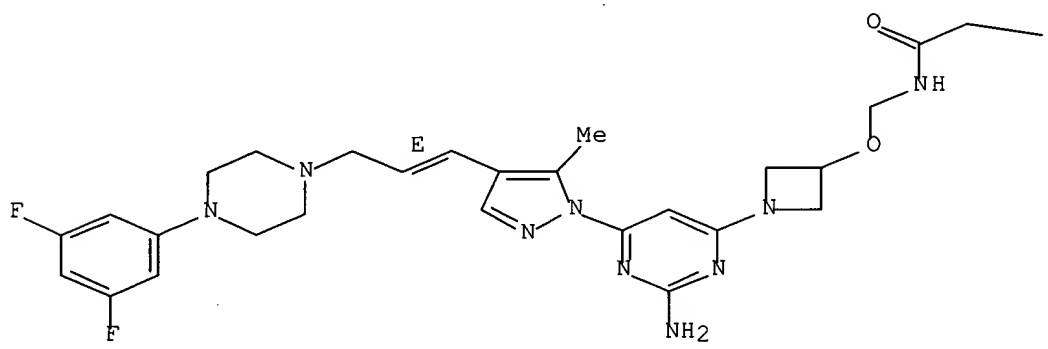


RN 401470-41-5 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-methionyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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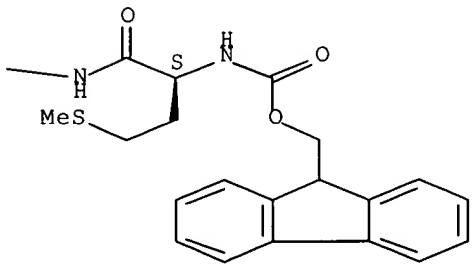
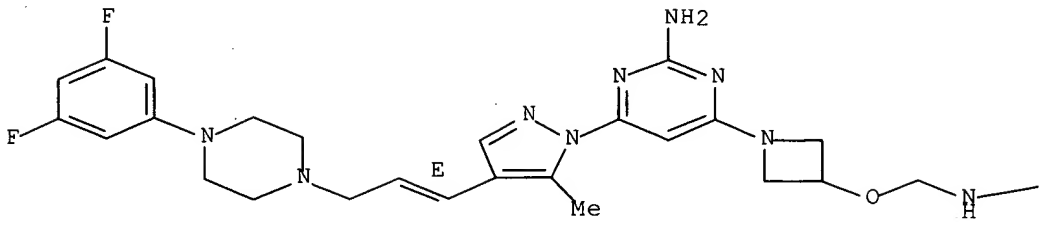


RN 401470-42-6 HCAPLUS
CN Glycinamide, L-methionyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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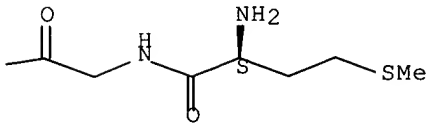
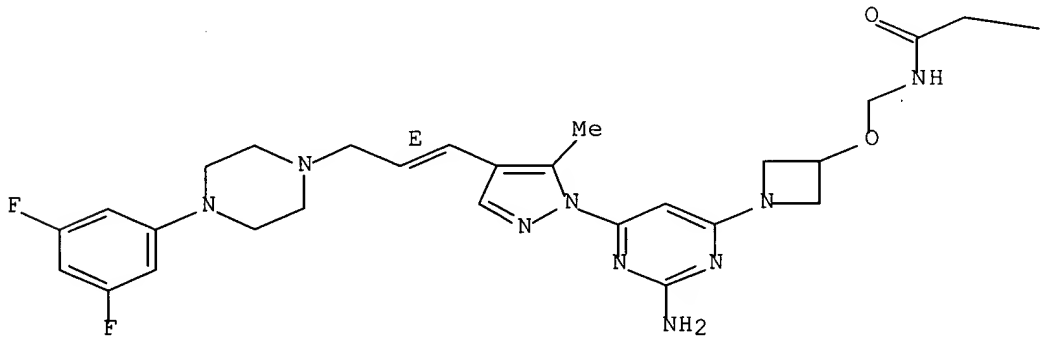


RN 401470-43-7 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-methionyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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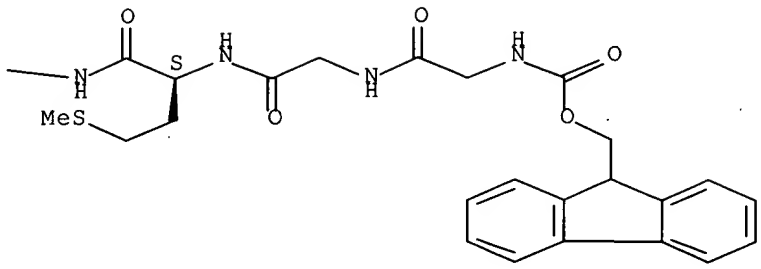
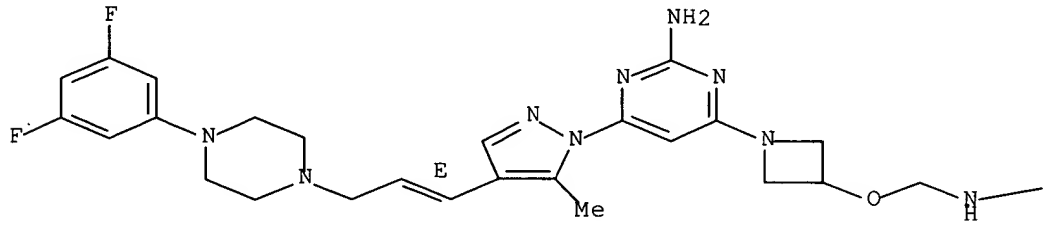


RN 401470-44-8 HCAPLUS
CN Glycinamide, glycylglycyl-L-methionyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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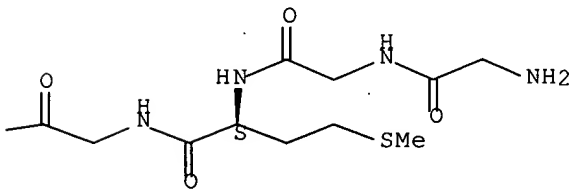
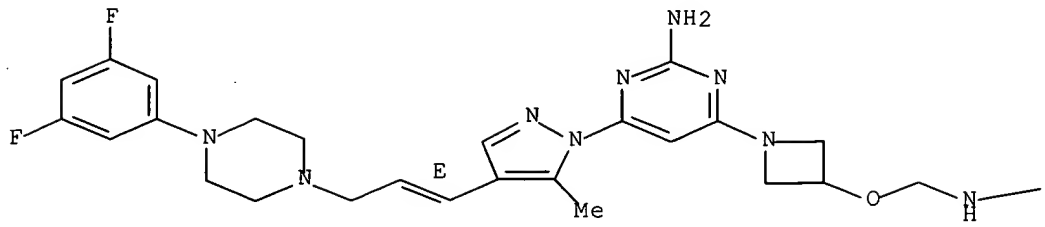


RN 401470-45-9 HCAPLUS
CN Carbamic acid, [2-[[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]amino]-2-oxoethyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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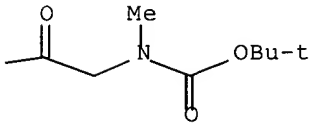
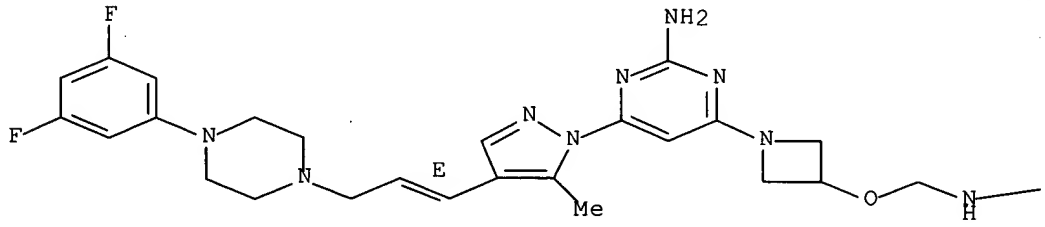


RN 401470-46-0 HCAPLUS
CN Acetamide, N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]-2-(methylamino)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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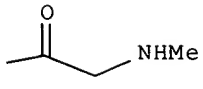
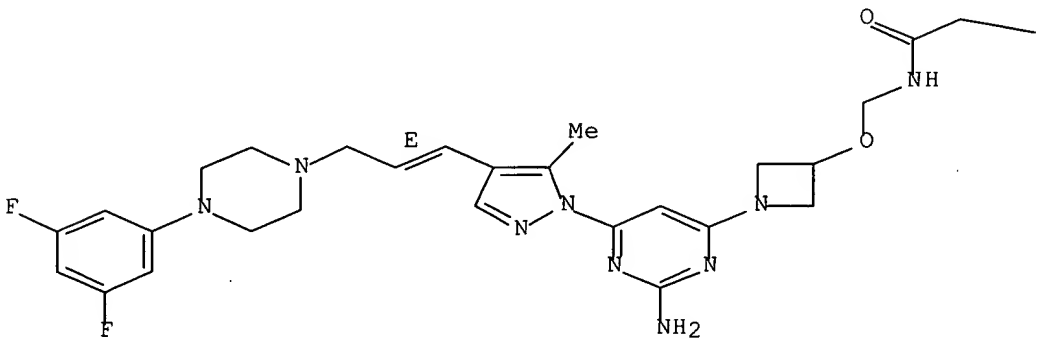


RN 401470-47-1 HCAPLUS
CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-

azetidinyl]oxy]methyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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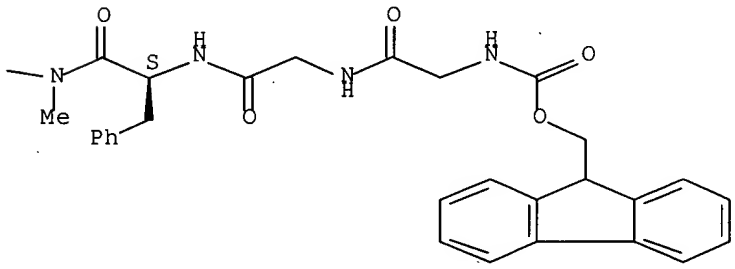
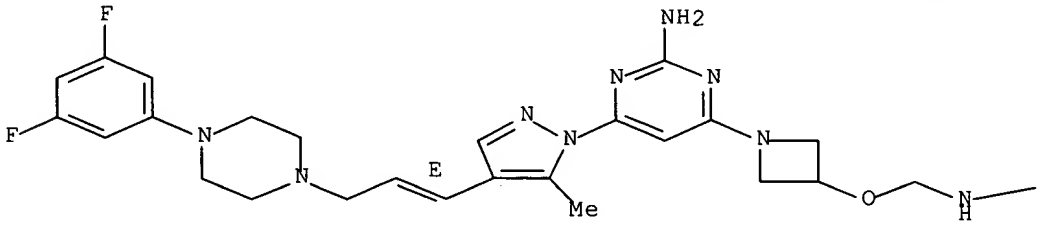


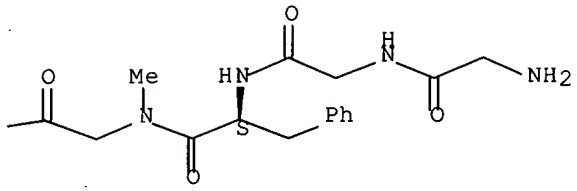
RN 401470-48-2 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



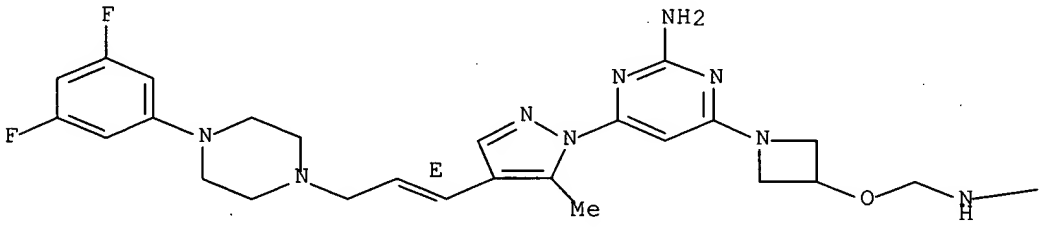
PAGE 1-B



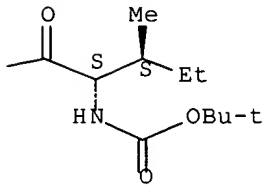
RN 401470-49-3 HCAPLUS
CN Carbamic acid, [(1S,2S)-1-[[[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]amino]carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



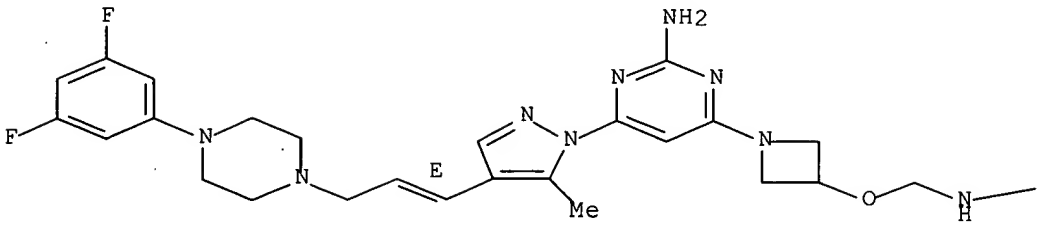
PAGE 1-B



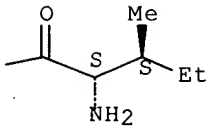
RN 401470-50-6 HCAPLUS
CN Pentanamide, 2-amino-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]-3-methyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



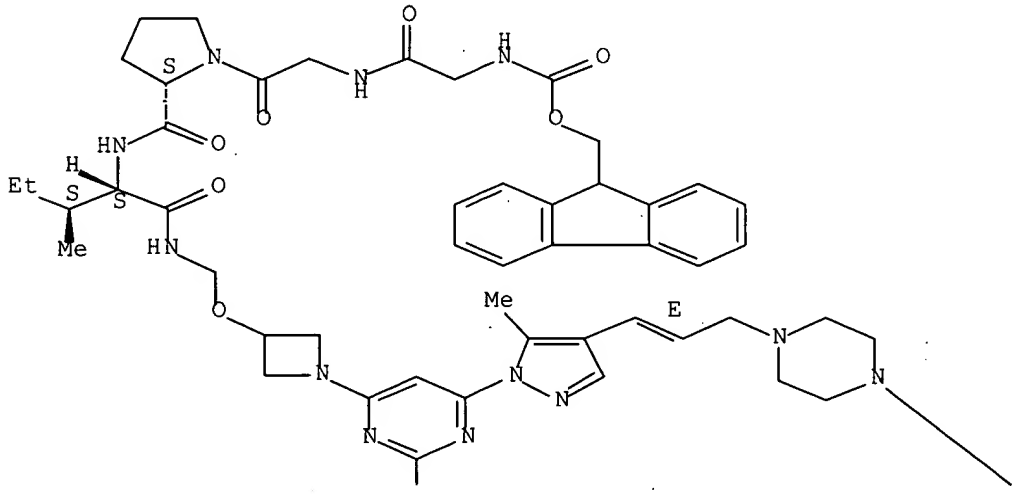
PAGE 1-B



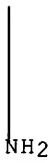
RN 401470-51-7 HCAPLUS
CN L-Isoleucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-prolyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

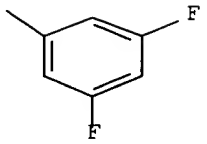
PAGE 1-A



PAGE 2-A



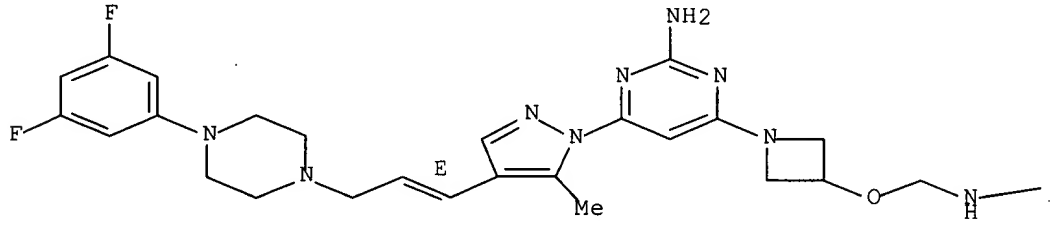
PAGE 2-B



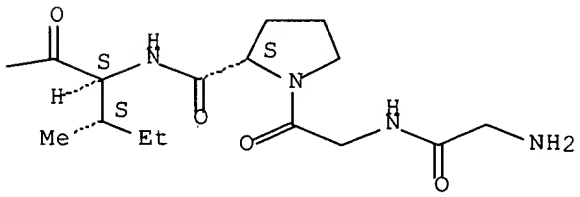
RN 401470-52-8 HCAPLUS
CN L-Isoleucinamide, glycylglycyl-L-prolyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

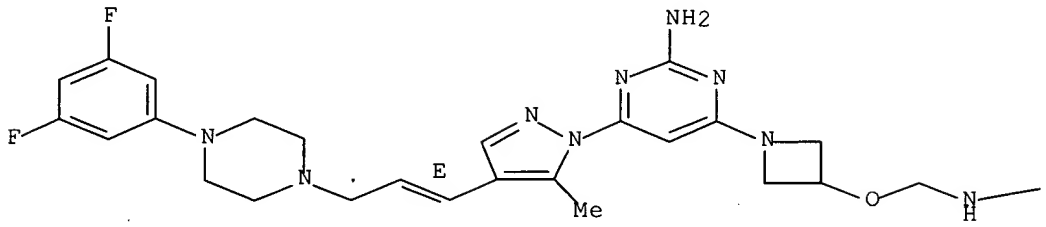


RN 401470-53-9 HCAPLUS
CN Carbamic acid, [(1S)-1-[[[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]amino]carbonyl]-3-methylbutyl]-,

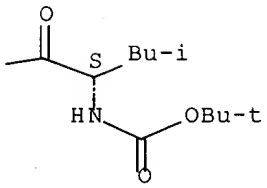
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



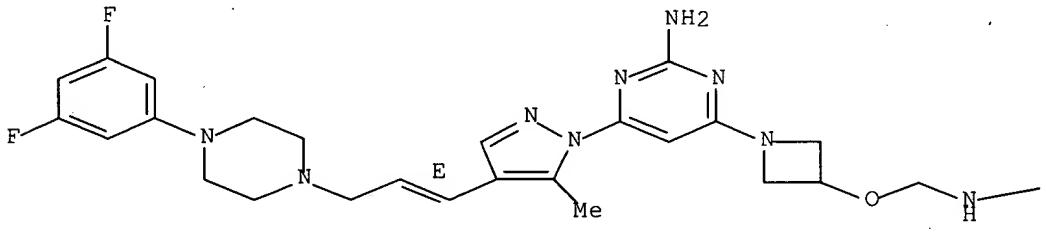
PAGE 1-B



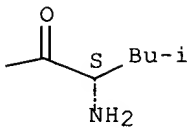
RN 401470-54-0 HCAPLUS
CN Pentanamide, 2-amino-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



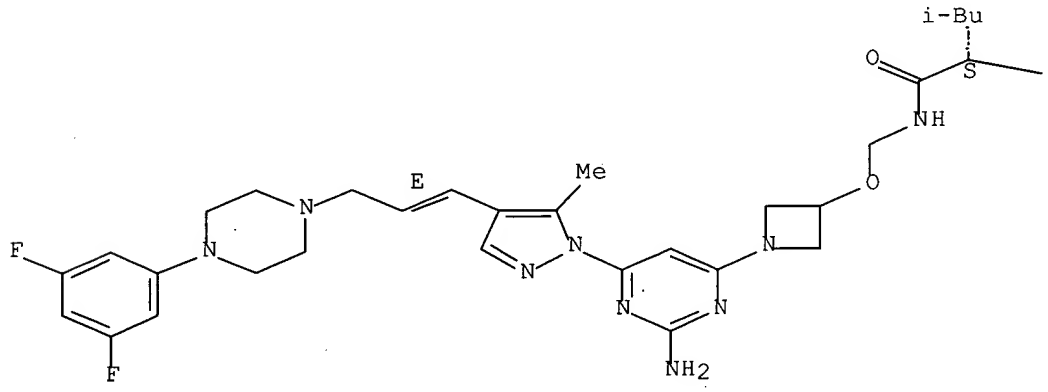
PAGE 1-B



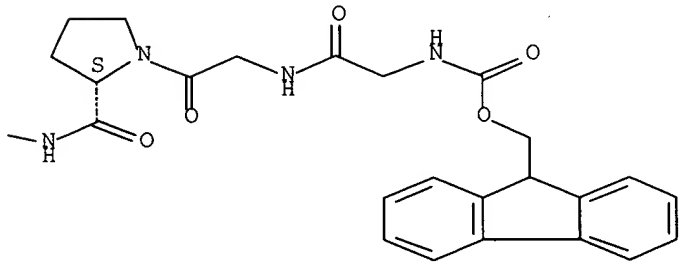
RN 401470-55-1 HCAPLUS
CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-prolyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



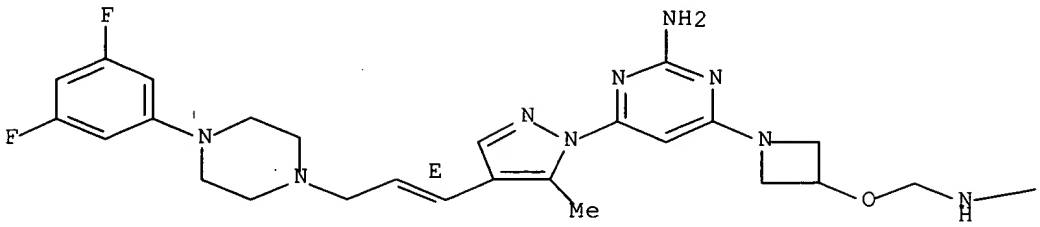
PAGE 1-B



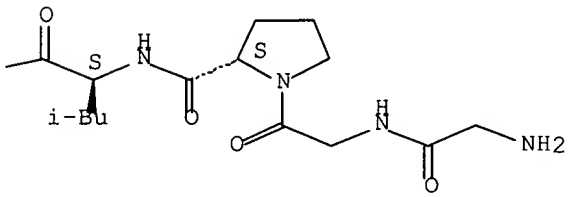
RN 401470-56-2 HCAPLUS
CN L-Leucinamide, glycylglycyl-L-prolyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

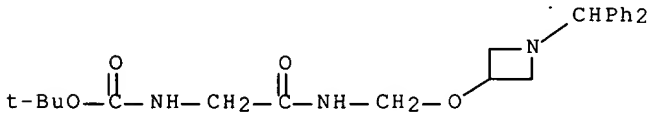
PAGE 1-A



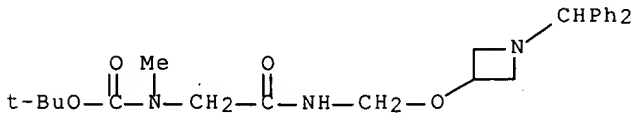
PAGE 1-B



RN 401470-58-4 HCAPLUS
CN Carbamic acid, [2-[[[[1-(diphenylmethyl)-3-azetidinyl]oxy]methyl]amino]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

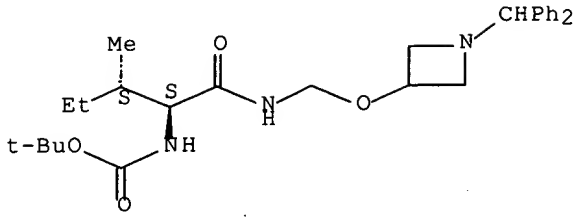


RN 401470-60-8 HCAPLUS
CN Carbamic acid, [2-[[[[1-(diphenylmethyl)-3-azetidinyl]oxy]methyl]amino]-2-oxoethyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



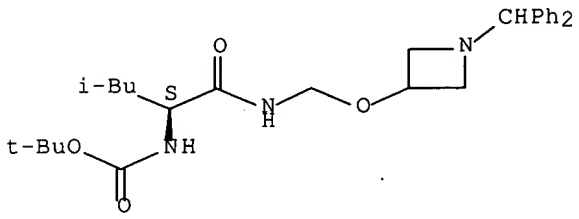
RN 401470-61-9 HCAPLUS
CN Carbamic acid, [(1S,2S)-1-[[[[[1-(diphenylmethyl)-3-azetidinyl]oxy]methyl]amino]carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 401470-62-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[[[[[1-(diphenylmethyl)-3-azetidinyl]oxy]methyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:669315 HCAPLUS
DOCUMENT NUMBER: 136:18928
TITLE: New antibody purification procedure using a thermally responsive poly(N-isopropylacrylamide)-dextran derivative conjugate
AUTHOR(S): Anastase-Ravion, S.; Ding, Z.; Pelle, A.; Hoffman, A. S.; Letourneur, D.
CORPORATE SOURCE: INVIMAT, Universite Paris 13, Villetaneuse, 93430, Fr.
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 761(2), 247-254
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

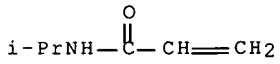
AB Through their specificity and affinity, antibodies are useful tools in research and medicine. In this study, we investigated a new type of chromatog. method using a thermosensitive polymer for the purifn. of antibodies against a dextran deriv. (DD), as a model. The thermally reversible sol.-insol. poly(N-isopropylacrylamide)-dextran deriv. **conjugate**, named poly(NIPAAm)-DD, has been synthesized by **conjugating** amino-terminated poly(N-isopropylacrylamide) to a DD via ethyl-3-(3-dimethylaminopropyl)-carbodiimide. On one hand, this report describes the two steps of poly(NIPAAm)-DD **conjugation** and characterization. On the other hand, the poly(NIPAAm)-DD **conjugate** was used as a tool to purify polyclonal antibodies in serum samples from rabbits s.c. immunized with the derivatized dextran. Antibodies were purified and quantified by immunoenzymic assays. Our results indicate that antibodies recognized both DD and poly(NIPAAm)-DD. In contrast, they did not bind to native poly(NIPAAm) or poly(NIPAAm) **conjugated** with another anionic dextran. We conclude that the

conjugation of a **polysaccharide** to poly(NIPAAm) leads to an original and efficient chromatog. method to purify antibodies. Moreover, this novel method of purifn. is rapid, sensitive, inexpensive and could be used to purify various types of antibodies.

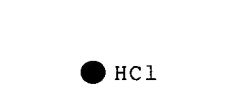
IT **25189-55-3**, Poly(N-isopropylacrylamide)
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(new antibody purifn. procedure using a thermally responsive poly(N-isopropylacrylamide)-dextran deriv. conjugate)
RN 25189-55-3 HCAPLUS
CN 2-Propenamide, N-(1-methylethyl)-, homopolymer (9CI) (CA INDEX NAME)

CM 1

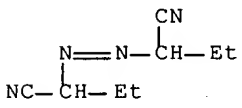
CRN 2210-25-5
CMF C6 H11 N O



IT **156-57-0**, 2-Aminoethanethiol hydrochloride **66205-07-0**, 2,2'-Azobisbutyronitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(new antibody purifn. procedure using a thermally responsive poly(N-isopropylacrylamide)-dextran deriv. conjugate)
RN 156-57-0 HCAPLUS
CN Ethanethiol, 2-amino-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



RN 66205-07-0 HCAPLUS
CN Butanenitrile, 2,2'-azobis- (9CI) (CA INDEX NAME)



IT **9044-05-7DP, Carboxymethyl dextran**, poly(N-isopropylacrylamide) **conjugates 25189-55-3DP**, Poly(N-isopropylacrylamide), **carboxymethyl dextran conjugates**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(new antibody purifn. procedure using a thermally responsive poly(N-isopropylacrylamide)-dextran deriv. **conjugate**)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

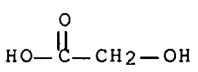
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

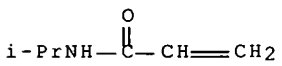
CRN 79-14-1
CMF C2 H4 O3



RN 25189-55-3 HCAPLUS
CN 2-Propenamide, N-(1-methylethyl)-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 2210-25-5
CMF C6 H11 N O



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:322648 HCAPLUS
DOCUMENT NUMBER: 135:185307
TITLE: Characteristics of tissue distribution of various polysaccharides as drug carriers: influences of molecular weight and anionic charge on tumor targeting
AUTHOR(S): Sugahara, Shuichi; Okuno, Satoshi; Yano, Toshiro; Hamana, Hiroshi; Inoue, Kazuhiro
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(5), 535-543
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using the Walker 256 model for carcinosarcoma-bearing rats, we i.v. administered 5 **polysaccharide** carriers with various mol. wts. (MWs) and elec. charges and tested for their plasma and tissue distribution. Two carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex), showed higher plasma AUC than the other carriers tested, namely, CMchitin (CMCh), N-desulfated N-acetylated heparin (DSH), and hyaluronic acid (HA). This was consistently found to be true over the range of MWs tested. For CMDex, the max. value of plasma AUC was obtained when the MW exceeded 150 kDa. As for the anionic charge, CMDex (110-180 kDa) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed max. plasma AUC values. Twenty-four hours after administration, the concn. of CMDex (180-250 kDa; DS: 0.6-1.2) in tumors

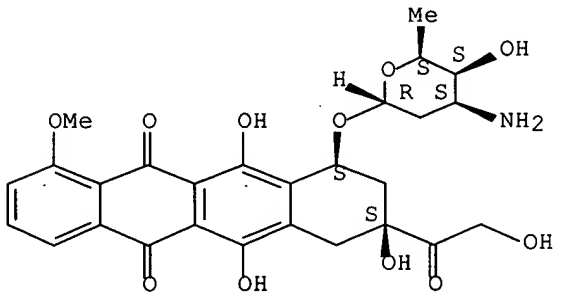
was more than 3% of dose/g-approx. 10-fold higher than those obsd. with CMCh, DSH and HA. Doxorubicin (DXR) was bound to these carriers via a peptide spacer, GlyGlyPheGly (GGFG), to give carrier-GGFG-DXR **conjugates** (DXR content: 4.2-7.0 (wt./wt.)%), and the antitumor effects of these **conjugates** were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor wts. after a single i.v. injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR **conjugates** significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and HA-GGFG-DXR **conjugates** in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR **conjugates** was related to the extent with which the carriers accumulated in the tumors.

IT **9067-32-7DP**, Hyaluronic acid sodium salt, **conjugates** with doxorubicin and peptide **23214-92-8DP**, Doxorubicin, **conjugates** with peptide and polysaccharides **39422-83-8DP**, **Carboxymethyl dextran** sodium salt, **conjugates** with doxorubicin and peptide **65667-26-7DP**, **conjugates** with doxorubicin and peptide **105156-94-3DP**, Carboxymethyl chitin sodium salt, **conjugates** with doxorubicin and peptide **200427-88-9DP**, **conjugates** with doxorubicin and polysaccharides **355129-33-8DP**, **conjugates** with doxorubicin and peptide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effects of mol. wt. and anionic charge of **polysaccharide** drug carriers on tumor targeting)

RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 23214-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 39422-83-8 HCAPLUS
CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

CM 1

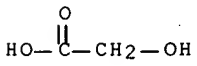
CRN 9004-54-0
CMF Unspecified

CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 65667-26-7 HCAPLUS
CN Heparamine, N-acetyl, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

RN 105156-94-3 HCAPLUS
CN Chitin, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

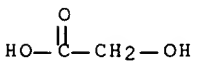
CM 1

CRN 1398-61-4
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

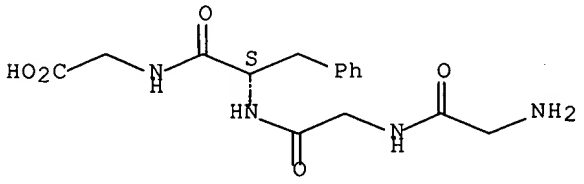
CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 200427-88-9 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 355129-33-8 HCAPLUS
CN D-Gluco-D-mannan, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

CM 1

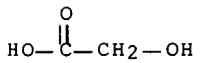
CRN 11078-31-2
CMF Unspecified

CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



IT **9067-32-7P**, Hyaluronic acid sodium salt **39422-83-8P**,
Carboxymethyl dextran sodium salt **65667-26-7P**
105156-94-3P, Carboxymethyl chitin sodium salt
355129-33-8P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(effects of mol. wt. and anionic charge of polysaccharide drug carriers on tumor targeting)
RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 39422-83-8 HCAPLUS
CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

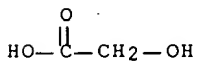
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 65667-26-7 HCAPLUS
CN Heparamine, N-acetyl, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 105156-94-3 HCAPLUS
CN Chitin, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

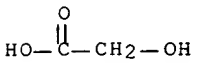
CM 1

CRN 1398-61-4
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 355129-33-8 HCAPLUS
CN D-Gluco-D-mannan, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

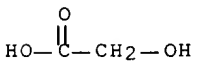
CM 1

CRN 11078-31-2
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



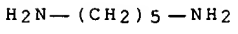
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:228007 HCAPLUS
DOCUMENT NUMBER: 133:109911
TITLE: Ionic **Polysaccharide** Hydrogels via the Passerini and Ugi Multicomponent Condensations: Synthesis, Behavior and Solid-State NMR Characterization
AUTHOR(S): De Nooy, Arjan E. J.; Capitani, Donatella; Masci, Giancarlo; Crescenzi, Vittorio
CORPORATE SOURCE: Department of Chemistry, University 'La Sapienza', Rome, 00185, Italy
SOURCE: Biomacromolecules (2000), 1(2), 259-267
CODEN: BOMAF6; ISSN: 1525-7797
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Original data are provided demonstrating that the title condensations are simple and versatile methods for the synthesis of hydrogels based on a variety of carboxylated polysaccharides. In this work, the biopolymers considered are sodium hyaluronate and sodium alginate. Nonnatural carboxylated polysaccharides were com. (carboxymethyl)cellulose or were obtained by carboxymethylation or selective oxidn. of primary alc. groups of scleroglucan and dextran. Hydrogels prepd. via the Passerini reaction

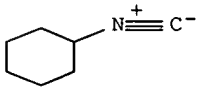
were transparent, alkali labile materials whereas the transparency of the Ugi gels depended on the **polysaccharide**, the cross-**linker**, and the degree of crosslinking. The Ugi gels were stable for several months at a pH ranging from 1.3 to 11 and up to temps. over 90 .degree.C. The structure of the networks was studied by means of 13C CP-MAS and 15N CP-MAS NMR spectroscopy. A quant. NMR anal. and elemental anal. of the dry gels allowed us to est. the efficiency of the reactions, i.e., the actual degree of crosslinking, which appeared to be about 80% of theor. The influence of added salt and pH on the swelling of several Ugi gels with different degrees of crosslinking was studied in a qual. manner.

IT **462-94-2**, 1,5-Pentanediamine **931-53-3**, Cyclohexyl isocyanide **2769-64-4**, Butyl isocyanide **4117-33-3**, L-Lysine ethyl ester **9004-32-4 9005-38-3**, Sodium alginate **9044-05-7**, Carboxymethyl dextran **9067-32-7**, Sodium hyaluronate **39464-87-4D**, Scleroglucan, oxidized **282730-55-6**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(prepn., behavior and solid-state NMR characterization of ionic **polysaccharide** hydrogels via the Passerini and Ugi multicomponent condensations)

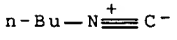
RN 462-94-2 HCAPLUS
CN 1,5-Pentanediamine (8CI, 9CI) (CA INDEX NAME)



RN 931-53-3 HCAPLUS
CN Cyclohexane, isocyano- (9CI) (CA INDEX NAME)

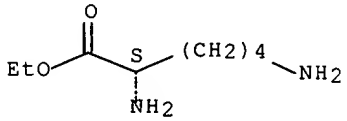


RN 2769-64-4 HCAPLUS
CN Butane, 1-isocyano- (9CI) (CA INDEX NAME)



RN 4117-33-3 HCAPLUS
CN L-Lysine, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 9004-32-4 HCAPLUS
CN Cellulose, carboxymethyl ether, sodium salt (8CI, 9CI) (CA INDEX NAME)

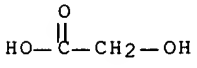
CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9005-38-3 HCAPLUS
CN Alginic acid, sodium salt (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

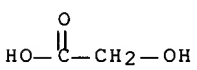
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 39464-87-4 HCAPLUS
CN Scleroglucan (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 282730-55-6 HCAPLUS
CN Scleroglucan, carboxymethyl ether (9CI) (CA INDEX NAME)

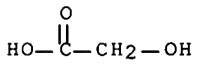
CM 1

CRN 39464-87-4
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

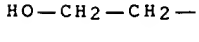
L47 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:684285 HCAPLUS
DOCUMENT NUMBER: 131:269259
TITLE: Affinity-type biosensor with gold surface, **linker** layer and hydrogel, and method for the fabrication
INVENTOR(S): Wischerhoff, Erik; Nicolaus, Thomas
PATENT ASSIGNEE(S): BioTul Bio Instruments G.m.b.H., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19817180	A1	19991021	DE 1998-19817180	19980417
DE 19817180	C2	20000427		

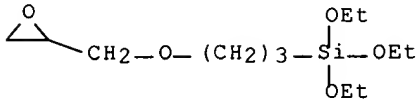
AB The invention concerns an affinity biosensor and its fabrication, that is composed of a gold surface, **linker** mols. and a bound hydrogel layer; the coverage of the surface is completed via hydrogen bonds and interactions of arom. rings upon sol-gel transformation. The **linker** mols. are of the general formula ARB; A = gold binding group, e.g. thio, disulfide, selenide, ; R = hydrocarbon chain, contg. at least two isolated phenol groups or heteroatoms; B = hydrogen binding group, e.g. hydroxy, epoxy, amino. Hydrogels are **polysaccharide** derivs., e.g. carboxymethyldextran. Alternately, the hydrogel is bound via a metal oxide layer to the **linker**.

IT **60-24-2**, Mercaptoethanol **2602-34-8**, Silane, [3-(2,3-epoxypropoxy)propyl]triethoxy- **5593-70-4** **6066-82-6**, N-Hydroxysuccinimide **7440-57-5**, Gold, uses **9044-05-7**, Carboxymethyldextran **17173-68-1**, Ethanamine, 2,2'-dithiobis-, hydrochloride **25952-53-8**, 1,3-Propanediamine, N'-(ethylcarbonimidoyl)-N,N-dimethyl-, monohydrochloride
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(affinity-type biosensor with gold surface, **linker** layer and hydrogel, and method for fabrication)

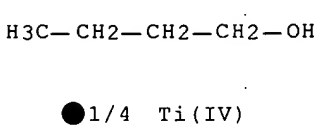
RN 60-24-2 HCAPLUS
CN Ethanol, 2-mercapto- (8CI, 9CI) (CA INDEX NAME)



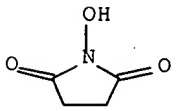
RN 2602-34-8 HCAPLUS
CN Silane, triethoxy[3-(oxiranylmethoxy)propyl]- (9CI) (CA INDEX NAME)



RN 5593-70-4 HCAPLUS
CN 1-Butanol, titanium(4+) salt (9CI) (CA INDEX NAME)



RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



RN 7440-57-5 HCAPLUS
CN Gold (8CI, 9CI) (CA INDEX NAME)

Au

RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

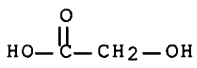
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

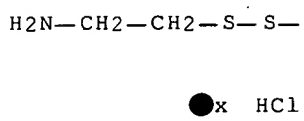
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

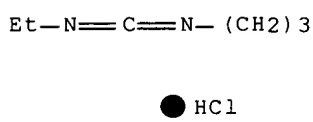
CRN 79-14-1
CMF C2 H4 O3



RN 17173-68-1 HCAPLUS
CN Ethanamine, 2,2'-dithiobis-, hydrochloride (9CI) (CA INDEX NAME)



RN 25952-53-8 HCAPLUS
CN 1,3-Propanediamine, N'-(ethylcarbonimidoyl)-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:9887 HCAPLUS
DOCUMENT NUMBER: 130:71612
TITLE: Bioresorbable antiadhesion of carboxypolysaccharide polyether intermacromolecular complexes and methods for their use in reducing surgical adhesions
INVENTOR(S): Schwartz, Herbert E.; Blackmore, John M.
PATENT ASSIGNEE(S): Fziomed, Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858011	A1	19981223	WO 1998-US10814	19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5906997	A	19990525	US 1997-877649	19970617
US 6017301	A	20000125	US 1998-23267	19980213
US 6034140	A	20000307	US 1998-23097	19980213
AU 9876985	A1	19990104	AU 1998-76985	19980528
EP 1002002	A1	20000524	EP 1998-924928	19980528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511897	T2	20020416	JP 1999-504437	19980528
US 6133325	A	20001017	US 1999-252147	19990218

PRIORITY APPLN. INFO.: US 1997-877649 A 19970617
WO 1998-US10814 W 19980528

AB The present invention relates to improved methods for making and using bioadhesive, bioresorbable, antiadhesion compns. made of intermacromol. complexes of carboxyl-contg. polysaccharides and polyethers, and to the resulting compns. The polymers are assocd. with each other, and are then either dried or are used as fluids. Bioresorbable, bioadhesive, antiadhesion compns. are useful in surgery to prevent the formation of post-surgical adhesions. The compns. are designed to breakdown in vivo, and thus be removed from the body. Membranes are inserted during surgery either dry or optionally after conditioning in aq. solns. The antiadhesion, bioadhesive, bioresorptive, antithrombogenic and phys. properties of such membranes can be varied as needed by carefully adjusting the pH of the polymer casting solns., polysaccharide compn., the polyether compn., or by conditioning the membranes prior to surgical use. Bi- or multi-layered membranes can be made and used to provide further control over the phys. and biol. properties of antiadhesion membranes. Antiadhesion compns. may also be used to deliver drugs to the surgical site and release them locally.

IT **1398-61-4**, Chitin **9000-69-5**, Pectin **9004-32-4**, Sodium CMC **9004-42-6**, Carboxyethyl cellulose **9004-61-9**, Hyaluronic acid **9005-25-8**, Starch, biological studies **9005-32-7**, Alginic acid **9005-49-6**, Heparin, biological studies **9005-79-2**, Glycogen, biological studies **9007-28-7**, Chondroitin sulfate **9044-05-7**, Carboxymethyl dextran **9050-30-0**, Heparan sulfate **25322-68-3**, **Polyethylene** oxide **83512-85-0**, Carboxymethyl chitosan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioresorbable adhesives contg. **carboxypolysaccharide** -polyether intermacromol. complexes)

RN 1398-61-4 HCAPLUS
CN Chitin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

RN 9000-69-5 HCAPLUS
CN Pectin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

RN 9004-32-4 HCAPLUS
CN Cellulose, carboxymethyl ether, sodium salt (8CI, 9CI) (CA INDEX NAME)

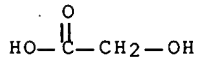
CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9004-42-6 HCAPLUS

CN Cellulose, 2-carboxyethyl ether (9CI) (CA INDEX NAME)

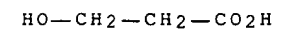
CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 503-66-2
CMF C3 H6 O3



RN 9004-61-9 HCAPLUS
CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9005-25-8 HCAPLUS
CN Starch (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9005-32-7 HCAPLUS
CN Alginic acid (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9005-49-6 HCAPLUS
CN Heparin (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9005-79-2 HCAPLUS
CN Glycogen (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9007-28-7 HCAPLUS
CN Chondroitin, hydrogen sulfate (9CI) (CA INDEX NAME)

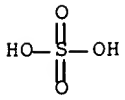
CM 1

CRN 9007-27-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 7664-93-9
CMF H2 O4 S



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

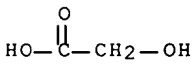
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9050-30-0 HCAPLUS
CN Heparan, sulfate (9CI) (CA INDEX NAME)

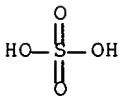
CM 1

CRN 70226-44-7
CMF Unspecified
CCI MAN

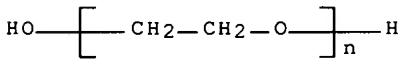
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 7664-93-9
CMF H2 O4 S



RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 83512-85-0 HCAPLUS
CN Chitosan, N-(carboxymethyl) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **7664-41-7**, Ammonia, uses
RL: NUU (Other use, unclassified); USES (Uses)
(membrane conditioning with; bioresorbable adhesives contg. carboxypolysaccharide-polyether intermacromol. complexes)
RN 7664-41-7 HCAPLUS
CN Ammonia (8CI, 9CI) (CA INDEX NAME)

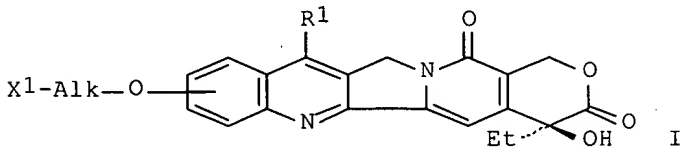
NH_3

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

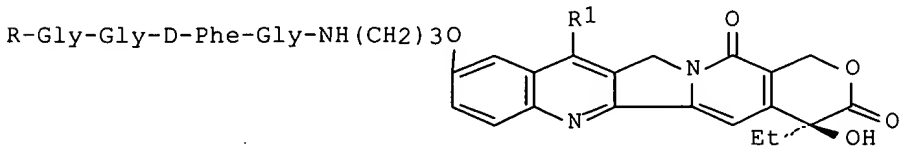
L47 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:665874 HCAPLUS
DOCUMENT NUMBER: 130:4084
TITLE: Preparation of **polysaccharide**-peptide or amino acid-linked camptothecin **conjugates** as antitumor agents
INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Akira; Yano, Toshiaki
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10273488	A2	19981013	JP 1998-16763	19980129
PRIORITY APPLN. INFO.:			JP 1997-17280	19970131

OTHER SOURCE(S): MARPAT 130:4084
GI



I



II

AB The title compds., which are camptothecin derives. [I; R1 =

(un)substituted lower alkyl; X1 = NHR2, OH; wherein R2 = H, lower alkyl; Alk = linear or branched alkylene optionally interrupted by O] linked to carboxy-contg. polysaccharide through a peptide or amino acid, are prepd. These compds. are reduced in toxicity and markedly enhanced in antitumor potency. Claimed is a pharmaceutical compn. contg. I as the active ingredient for treatment of cancers of lung, uterus, ovary, breast, digestive organs (large intestine, stomach, or pancreas), liver, kidney, prostate gland, and neck, malignant lymphoma, and leukemia. Thus, N-peptidyl-10-(3-aminopropoxy)-(20S)-camptothecin deriv. (II; R = H) (prepn. given) was condensed with carboxymethyl dextran sodium salt using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in H2O to give the title compd. II (R = carboxymethyl dextran sodium salt residue), which at 60 mg/kg (single dosage) in vivo inhibited 100% the proliferation of human breast cancer MX-1 cell in mice within 26 days after the drug administration.

IT **39422-83-8DP, Carboxymethyl dextran** sodium salt, **conjugates** with peptide-linked camptothecin derivs. **53571-87-2DP**, Carboxymethyl pullulan, **conjugates** with peptide-linked camptothecin derivs., sodium salt **187793-65-3P 187793-71-1P 187794-13-4P 187794-21-4P 187794-24-7P 187794-27-0P 187794-30-5P 187794-33-8P 187794-36-1P 187803-18-5DP**, bound to **carboxymethyl dextran** sodium salt **187803-20-9DP**, bound to **carboxymethyl dextran** sodium salt **187803-21-0DP**, bound to **carboxymethyl dextran** sodium salt **187803-22-1DP**, bound to **carboxymethyl dextran** sodium salt **187803-23-2DP**, bound to **carboxymethyl dextran** sodium salt **187803-26-5DP**, bound to **carboxymethyl dextran** sodium salt **187803-27-6DP**, bound to **carboxymethyl dextran** sodium salt **187803-28-7DP**, bound to **carboxymethyl dextran** sodium salt **187803-29-8DP**, bound to **carboxymethyl dextran** sodium salt **187803-30-1DP**, bound to **carboxymethyl dextran** sodium salt **187803-31-2DP**, bound to **carboxymethyl dextran** sodium salt **187803-32-3DP**, bound to **carboxymethyl dextran** sodium salt **187803-33-4DP**, bound to **carboxymethyl dextran** sodium salt **187803-34-5DP**, bound to **carboxymethyl dextran** sodium salt **187803-35-6DP**, bound to **carboxymethyl dextran** sodium salt **215591-97-2DP**, bound to **carboxymethyl dextran** sodium salt **215591-98-3DP**, bound to **carboxymethyl dextran** sodium salt **215592-03-3P 215592-06-6P 215592-09-9P 215592-15-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of **polysaccharide**-peptide or amino acid-linked camptothecin **conjugates** as antitumor agents)

RN 39422-83-8 HCAPLUS

CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

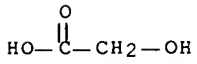
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 53571-87-2 HCAPLUS
CN Pullulan, carboxymethyl ether (9CI) (CA INDEX NAME)

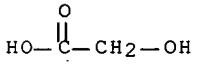
CM 1

CRN 9057-02-7
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

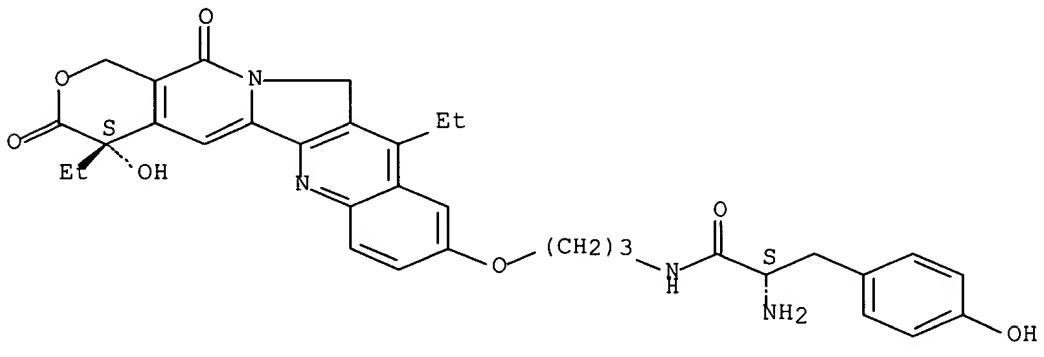
CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 187793-65-3 HCAPLUS
CN Benzenepropanamide, .alpha.-amino-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-4-hydroxy-, monohydrochloride, (.alpha.S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

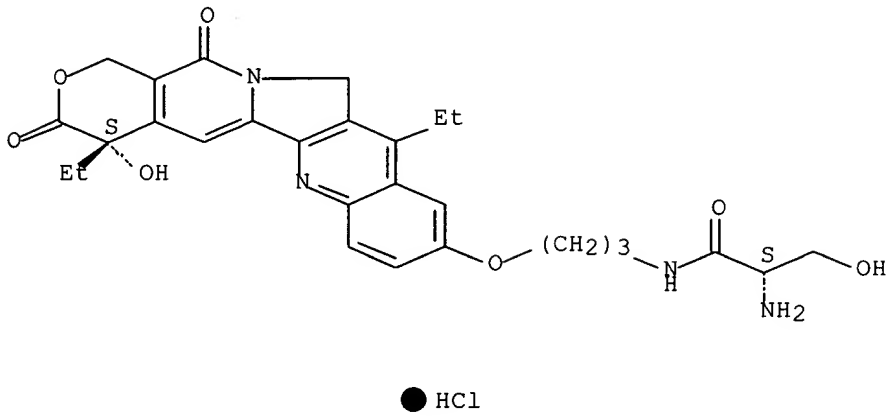


● HCl

RN 187793-71-1 HCAPLUS
CN Propanamide, 2-amino-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-

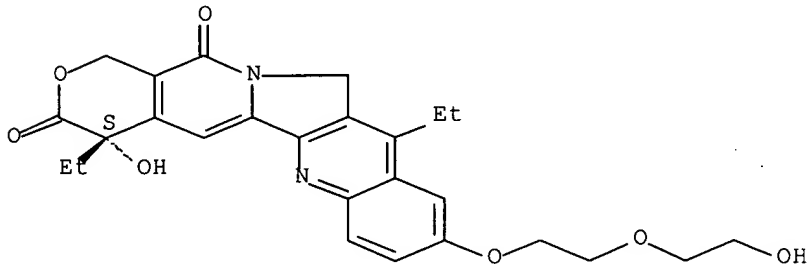
yl]oxy]propyl]-3-hydroxy-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



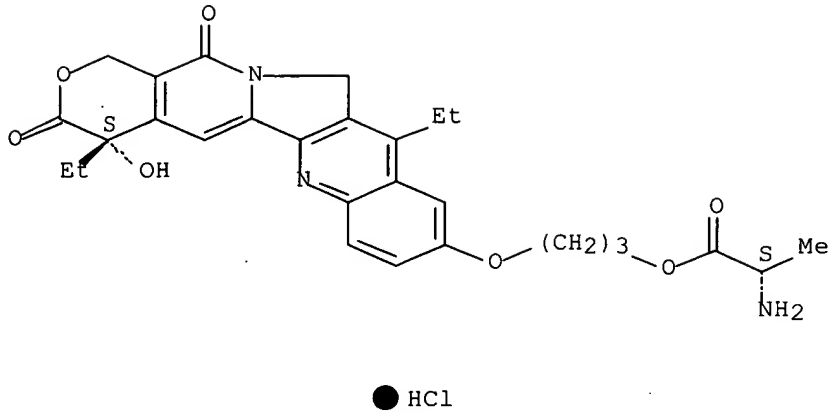
RN 187794-13-4 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4-hydroxy-9-[2-(2-hydroxyethoxy)ethoxy]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187794-21-4 HCAPLUS
CN L-Alanine, 3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl ester, monohydrochloride (9CI) (CA INDEX NAME)

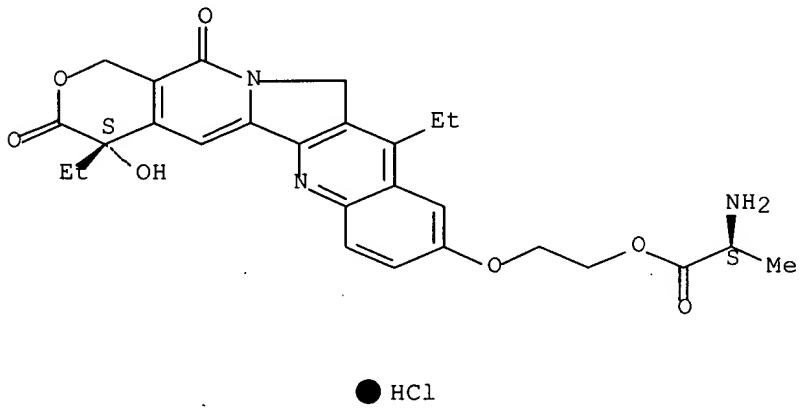
Absolute stereochemistry.



● HCl

RN 187794-24-7 HCAPLUS
CN L-Alanine, 2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

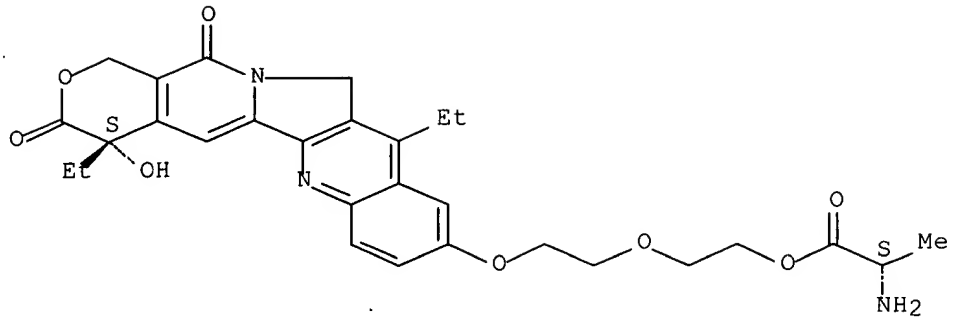
Absolute stereochemistry.



● HCl

RN 187794-27-0 HCAPLUS
CN L-Alanine, 2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

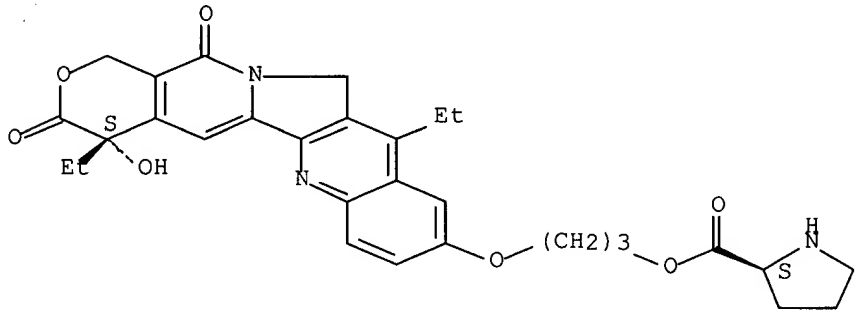
Absolute stereochemistry.



● HCl

RN 187794-30-5 HCAPLUS
CN L-Proline, 3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl ester, monohydrochloride (9CI) (CA INDEX NAME)

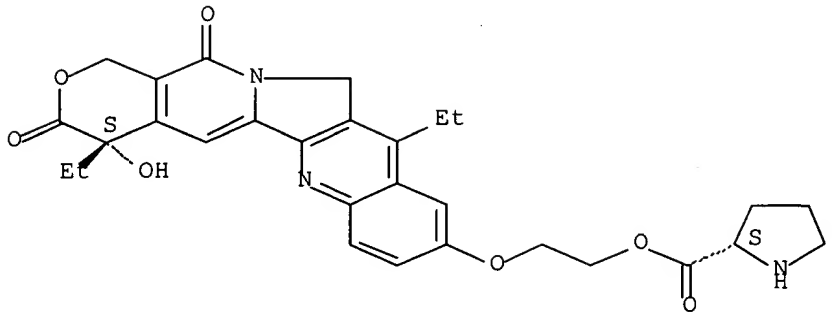
Absolute stereochemistry.



● HCl

RN 187794-33-8 HCAPLUS
CN L-Proline, 2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

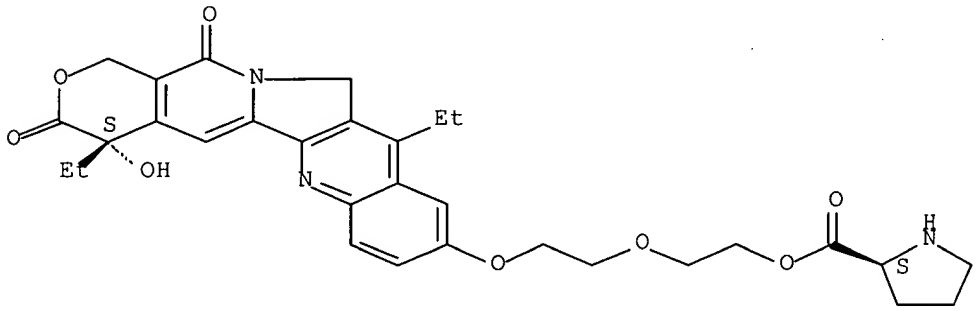
Absolute stereochemistry.



● HCl

RN 187794-36-1 HCAPLUS
CN L-Proline, 2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

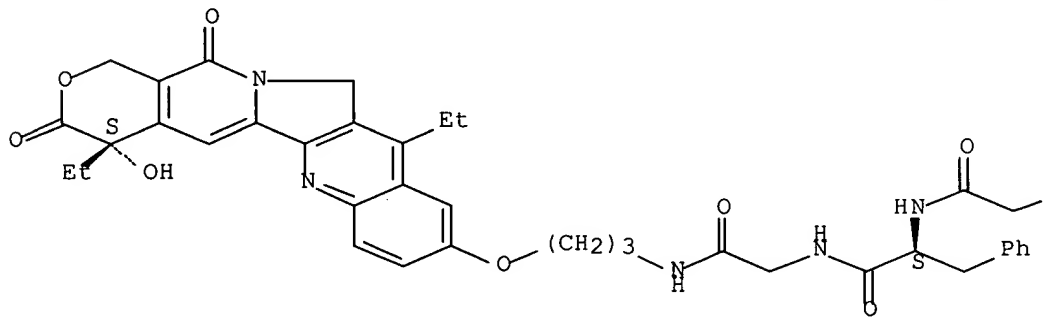


● HCl

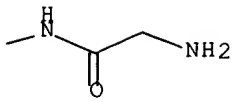
RN 187803-18-5 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

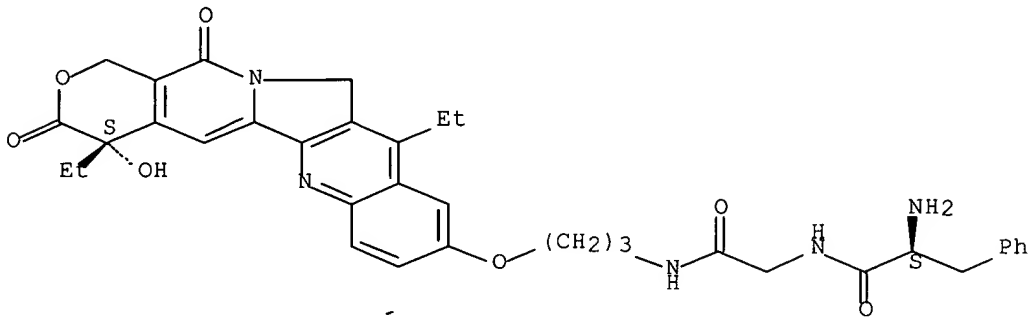


PAGE 1-B



RN 187803-20-9 HCAPLUS
CN Glycinamide, L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

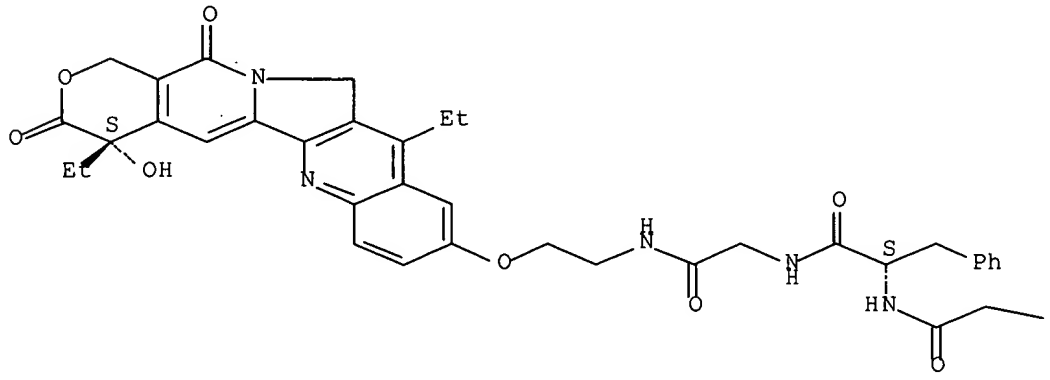
Absolute stereochemistry.



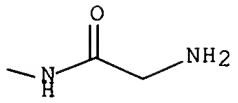
RN 187803-21-0 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



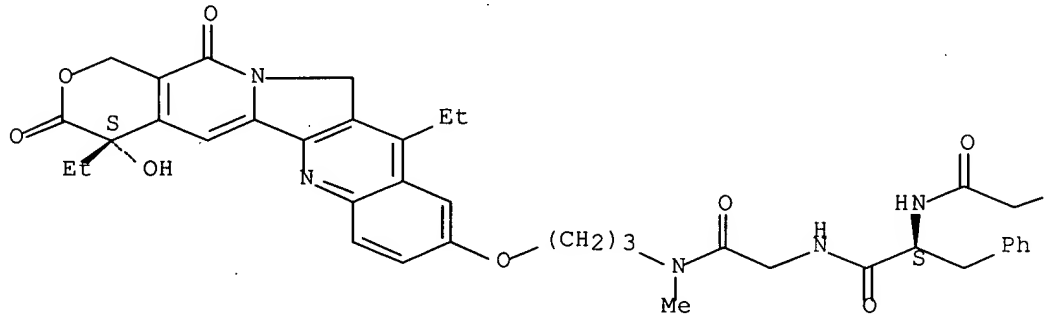
PAGE 1-B



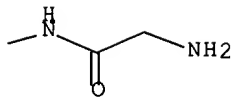
RN 187803-22-1 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



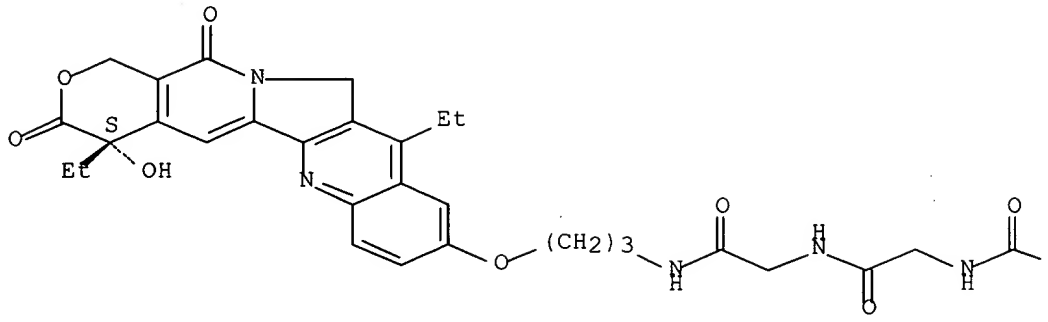
PAGE 1-B



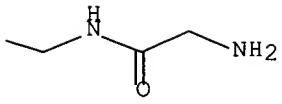
RN 187803-23-2 HCAPLUS
CN Glycinamide, glycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



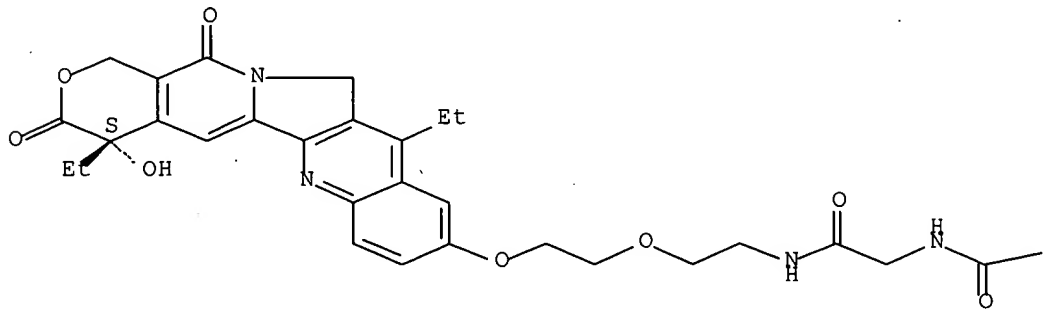
PAGE 1-B



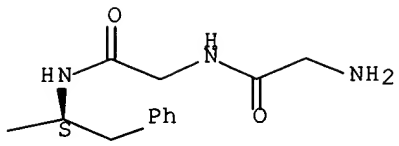
RN 187803-26-5 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



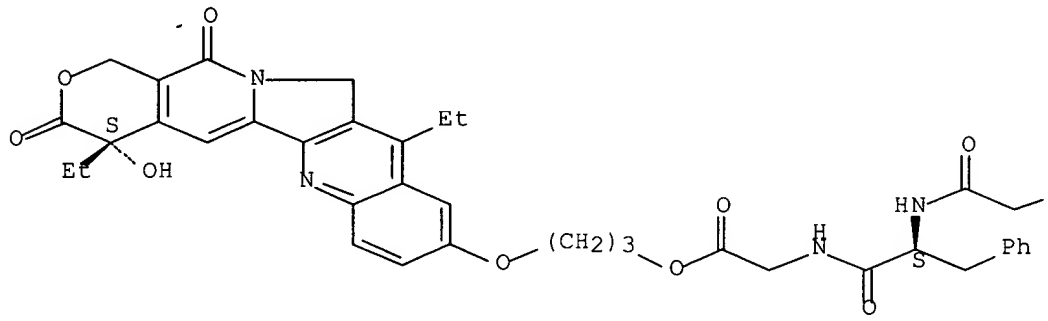
PAGE 1-B



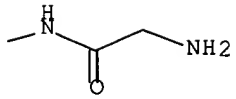
RN 187803-27-6 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl-, 3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

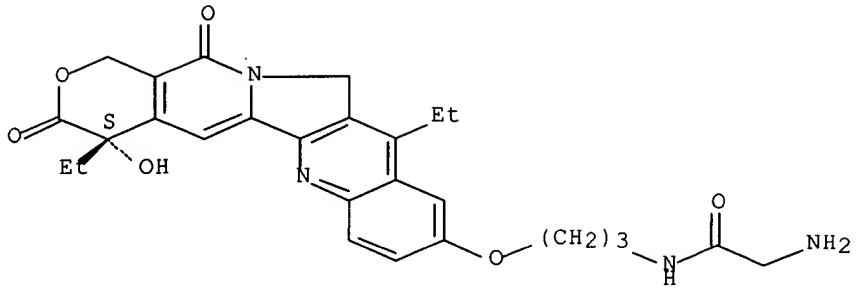


PAGE 1-B



RN 187803-28-7 HCAPLUS
CN Acetamide, 2-amino-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-(9CI) (CA INDEX NAME)

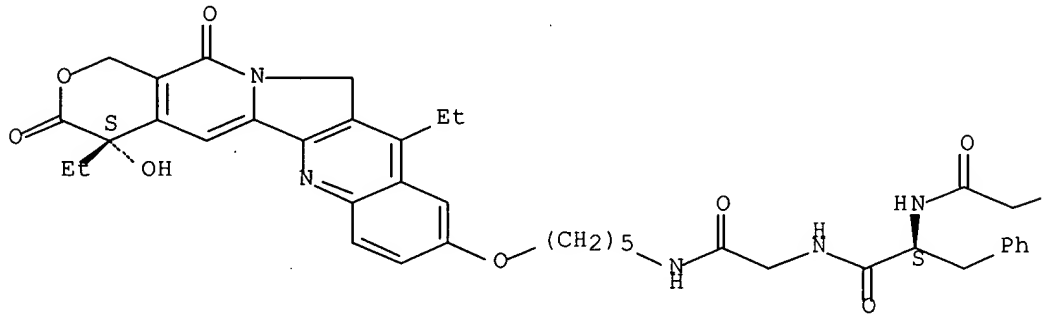
Absolute stereochemistry.



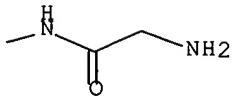
RN 187803-29-8 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[5-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



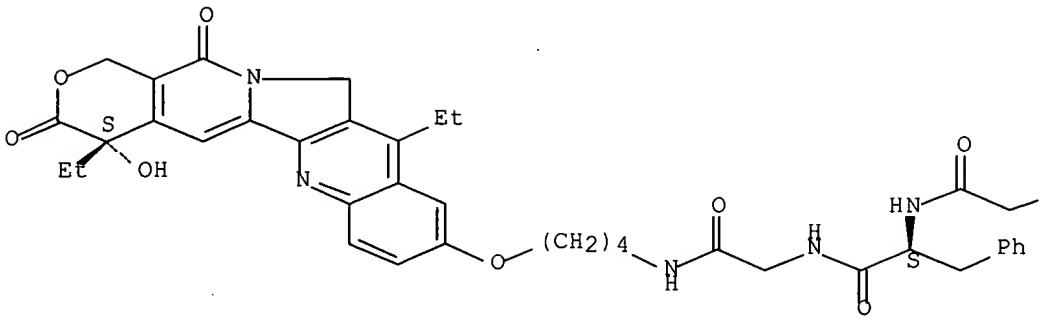
PAGE 1-B



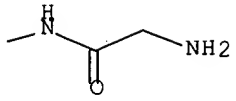
RN 187803-30-1 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[4-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

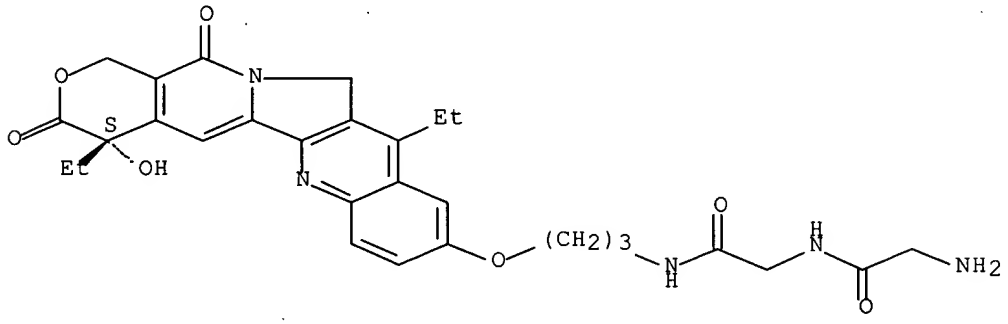


PAGE 1-B



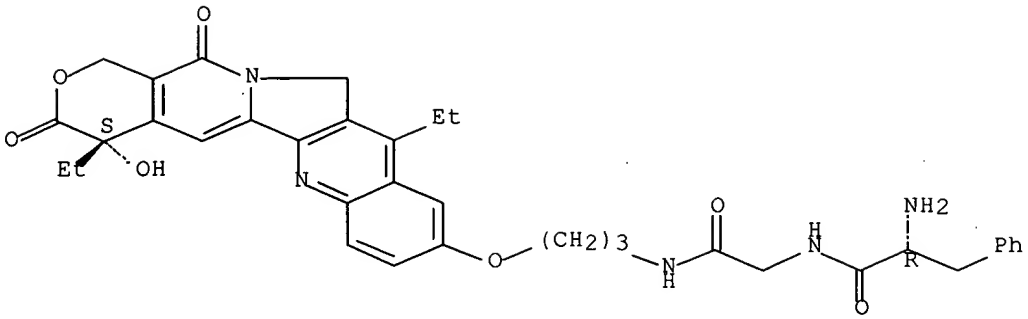
RN 187803-31-2 HCAPLUS
CN Glycinamide, glycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187803-32-3 HCAPLUS
CN Glycinamide, D-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

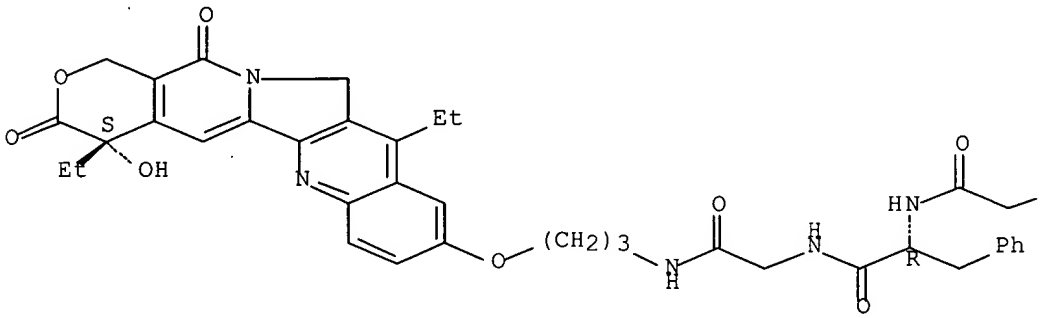
Absolute stereochemistry.



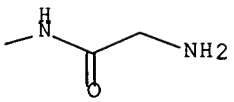
RN 187803-33-4 HCAPLUS
CN Glycinamide, glycylglycyl-D-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



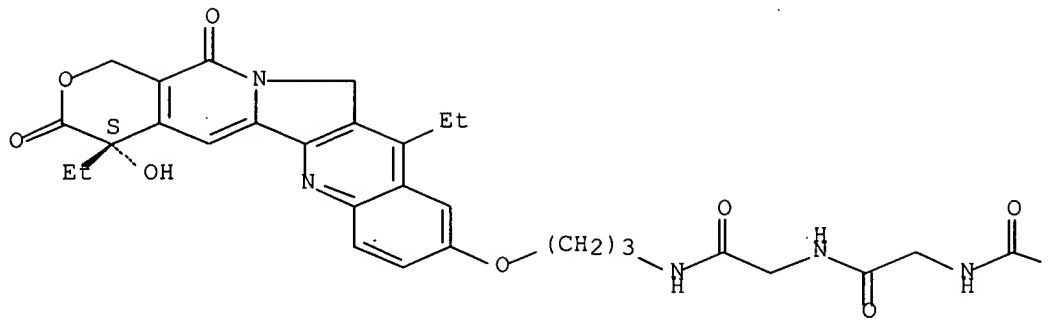
PAGE 1-B



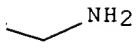
RN 187803-34-5 HCAPLUS
CN Glycinamide, glycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



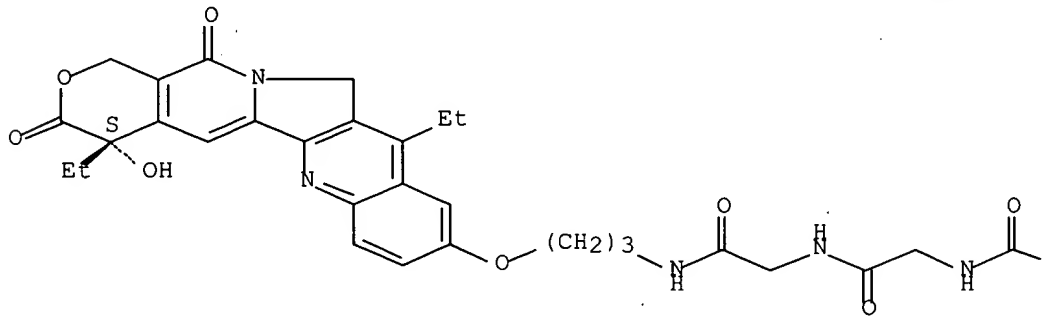
PAGE 1-B



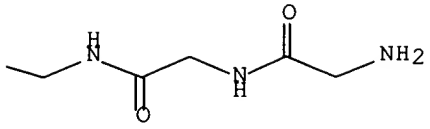
RN 187803-35-6 HCAPLUS
CN Glycinamide, glycylglycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

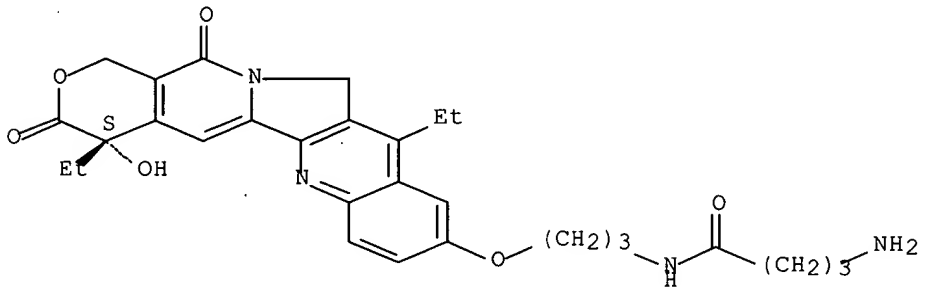


PAGE 1-B



RN 215591-97-2 HCAPLUS
CN Butanamide, 4-amino-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 215591-98-3 HCAPLUS
CN Butanamide, 4-[(4-amino-1-oxobutyl)amino]-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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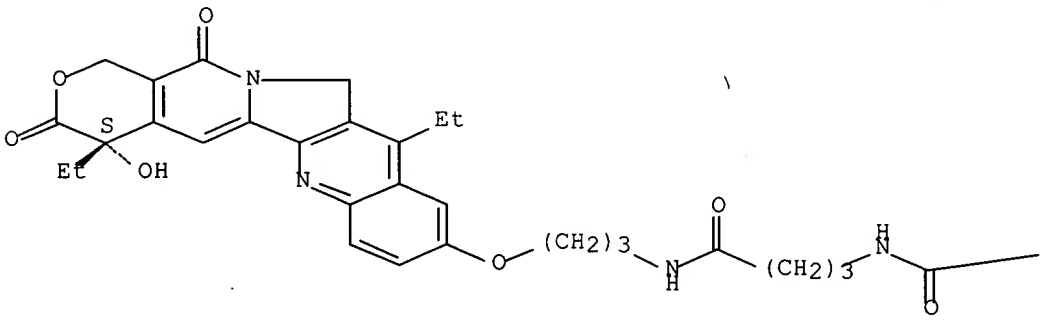
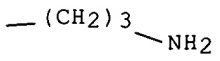
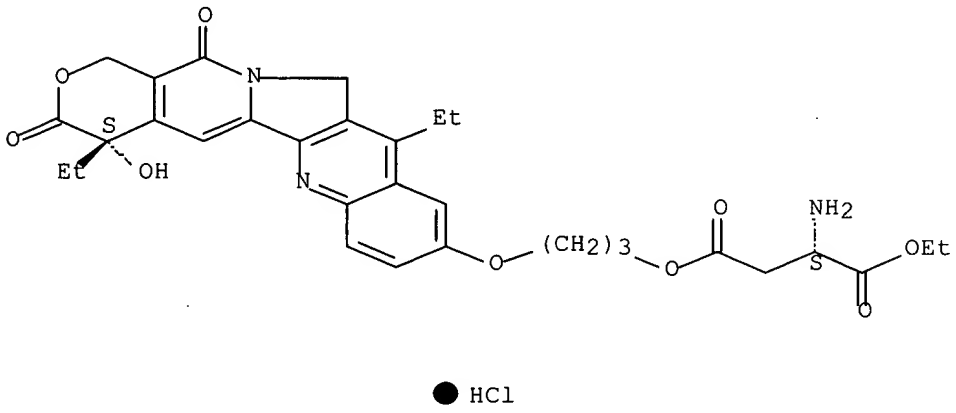




RN 215592-03-3 HCAPLUS
CN L-Aspartic acid, 4-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl] 1-ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

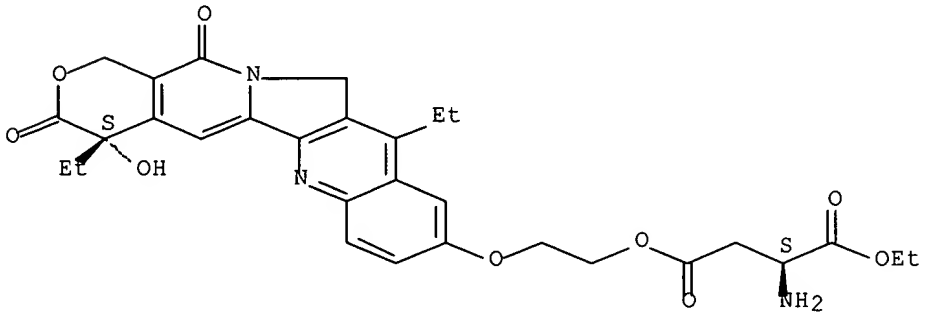
Absolute stereochemistry.



● HCl

RN 215592-06-6 HCAPLUS
CN L-Aspartic acid, 4-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl] 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 215592-09-9 HCAPLUS
CN L-Aspartic acid, 4-[2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl] 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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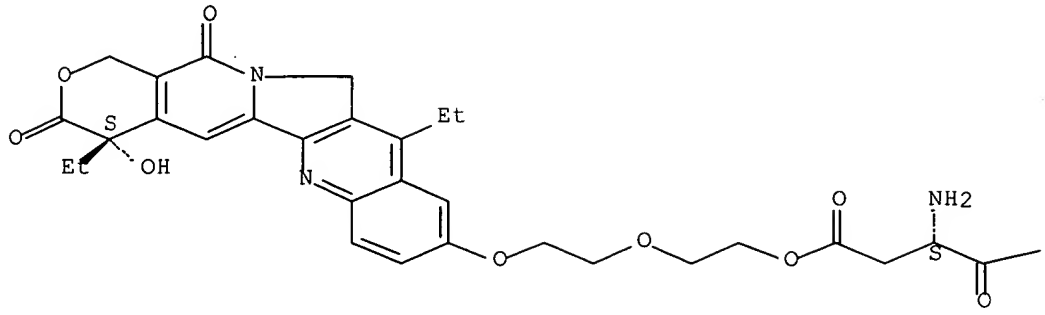

PAGE 1-B

—OEt

RN 215592-15-7 HCAPLUS
CN Glycinamide, glycyl-L-phenylalanylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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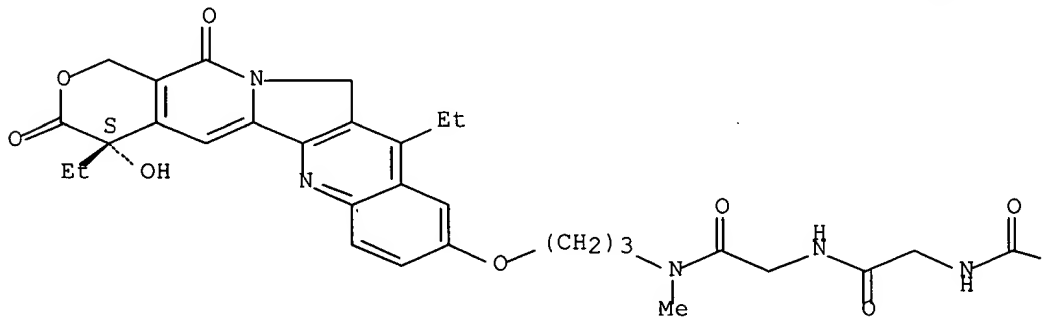
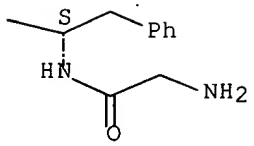
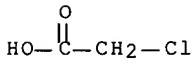


● HCl

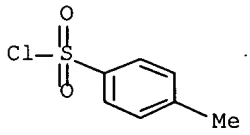


IT **79-11-8**, Chloroacetic acid, reactions **98-59-9**, Tosyl chloride **156-87-6**, 3-Aminopropanol **627-30-5**, 3-Chloropropanol **1826-67-1**, Vinylmagnesium bromide **3978-80-1 9004-54-0**, Dextran, reactions **9057-02-7**, Pullulan **15761-38-3 17302-47-5 18162-48-6**, tert-Butyldimethylsilyl chloride **24424-99-5**, Di-tert-butyl dicarbonate **28782-81-2 42454-06-8**, 5-Hydroxy-2-nitrobenzaldehyde **110351-94-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **polysaccharide**-peptide or amino acid-linked camptothecin **conjugates** as antitumor agents)

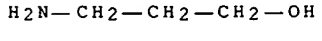
RN 79-11-8 HCAPLUS
CN Acetic acid, chloro- (8CI, 9CI) (CA INDEX NAME)



RN 98-59-9 HCAPLUS
CN Benzenesulfonyl chloride, 4-methyl- (9CI) (CA INDEX NAME)



RN 156-87-6 HCAPLUS
CN 1-Propanol, 3-amino- (8CI, 9CI) (CA INDEX NAME)



RN 627-30-5 HCAPLUS
CN 1-Propanol, 3-chloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

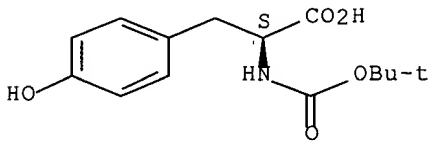
Cl—CH2—CH2—CH2—OH

RN 1826-67-1 HCAPLUS
CN Magnesium, bromoethenyl- (9CI) (CA INDEX NAME)

H2C═CH—Mg—Br

RN 3978-80-1 HCAPLUS
CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

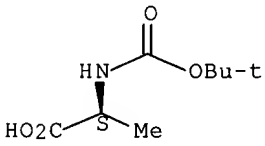


RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

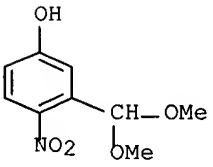
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9057-02-7 HCAPLUS
CN Pullulan (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 15761-38-3 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]- (9CI) (CA INDEX NAME)

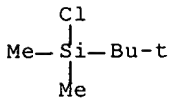
Absolute stereochemistry.



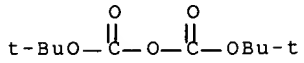
RN 17302-47-5 HCAPLUS
CN Phenol, 3-(dimethoxymethyl)-4-nitro- (9CI) (CA INDEX NAME)



RN 18162-48-6 HCAPLUS
CN Silane, chloro(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)

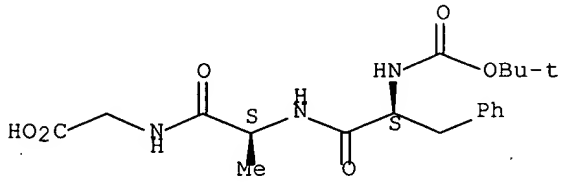


RN 24424-99-5 HCAPLUS
CN Dicarbonic acid, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

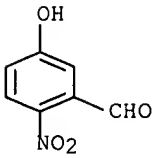


RN 28782-81-2 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

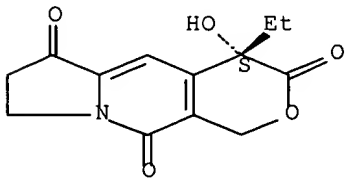


RN 42454-06-8 HCAPLUS
CN Benzaldehyde, 5-hydroxy-2-nitro- (7CI, 9CI) (CA INDEX NAME)



RN 110351-94-5 HCAPLUS
CN 1H-Pyrano[3,4-f]indolizine-3,6,10(4H)-trione, 4-ethyl-7,8-dihydro-4-hydroxy-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **39422-83-8P, Carboxymethyl dextran** sodium salt
53571-87-2DP, Carboxymethyl pullulan, sodium salt
58885-58-8P 80909-96-2P 187793-42-6P
187793-43-7P 187793-44-8P 187793-46-0P
187793-48-2P 187793-52-8P 187793-56-2P

187793-58-4P 187793-60-8P 187793-62-0P
187793-67-5P 187793-69-7P 187793-76-6P
187793-80-2P 187793-82-4P 187793-84-6P
187793-86-8P 187794-01-0P 187794-03-2P
187794-05-4P 187794-07-6P 187794-09-8P
187794-11-2P 187794-17-8P 187794-19-0P
187794-20-3P 187794-22-5P 187794-23-6P
187794-25-8P 187794-26-9P 187794-28-1P
187794-29-2P 187794-31-6P 187794-32-7P
187794-34-9P 187794-35-0P 187794-47-4P
187794-50-9P 187794-55-4P 187794-58-7P
187794-60-1P 187794-66-7P 187794-68-9P
187794-70-3P 187794-72-5P 187794-74-7P
187803-36-7P 187803-37-8P 205647-87-6P
215591-99-4P 215592-00-0P 215592-01-1P
215592-02-2P 215592-04-4P 215592-05-5P
215592-07-7P 215592-08-8P 215592-10-2P
215592-11-3P 215592-12-4P 215592-13-5P
215592-14-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **polysaccharide**-peptide or amino acid-linked camptothecin **conjugates** as antitumor agents)

RN 39422-83-8 HCAPLUS
CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

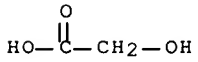
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 53571-87-2 HCAPLUS
CN Pullulan, carboxymethyl ether (9CI) (CA INDEX NAME)

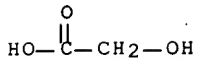
CM 1

CRN 9057-02-7
CMF Unspecified
CCI PMS, MAN

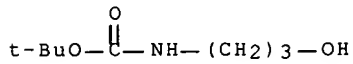
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

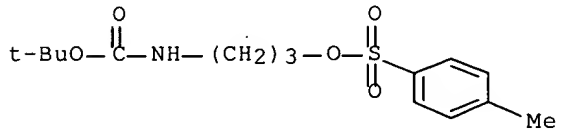
CRN 79-14-1
CMF C2 H4 O3



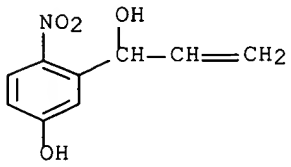
RN 58885-58-8 HCAPLUS
CN Carbamic acid, (3-hydroxypropyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



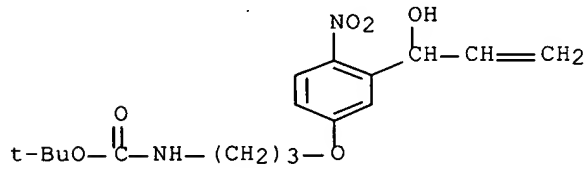
RN 80909-96-2 HCAPLUS
CN Carbamic acid, [3-[[(4-methylphenyl)sulfonyl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



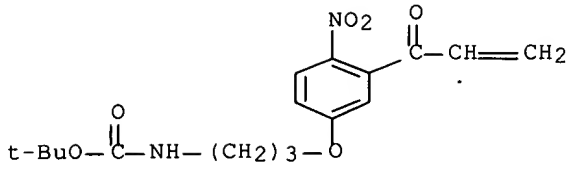
RN 187793-42-6 HCAPLUS
CN Benzenemethanol, .alpha.-ethenyl-5-hydroxy-2-nitro- (9CI) (CA INDEX NAME)



RN 187793-43-7 HCAPLUS
CN Carbamic acid, [3-[3-(1-hydroxy-2-propenyl)-4-nitrophenoxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

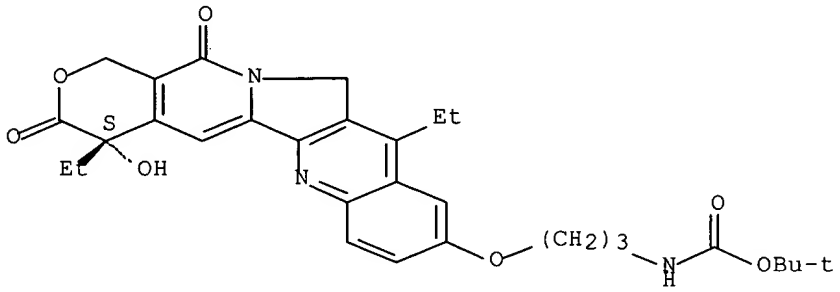


RN 187793-44-8 HCAPLUS
CN Carbamic acid, [3-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



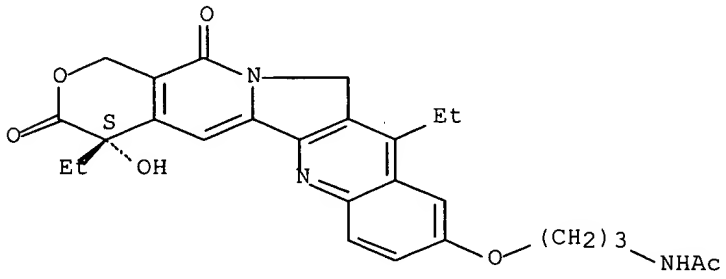
RN 187793-46-0 HCAPLUS
CN Carbamic acid, [3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



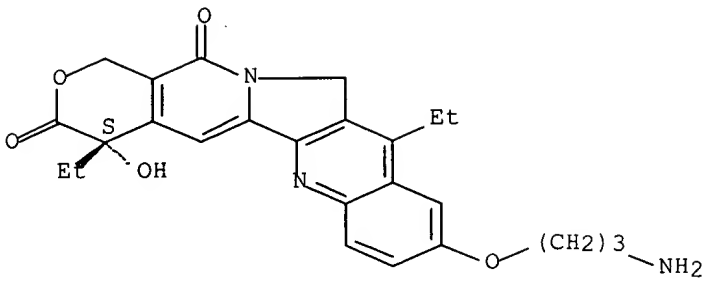
RN 187793-48-2 HCAPLUS
CN Acetamide, N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187793-52-8 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-(3-aminopropoxy)-4,11-diethyl-4-hydroxy-, monohydrochloride, (4S)- (9CI) (CA INDEX NAME)

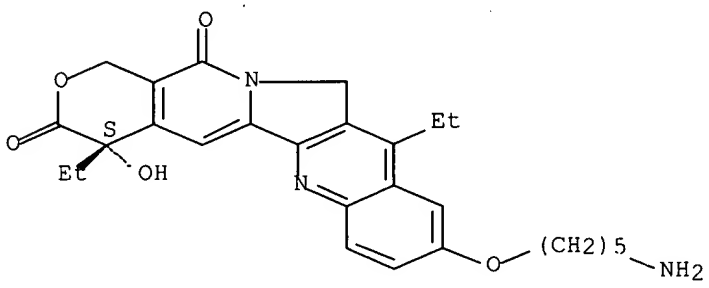
Absolute stereochemistry. Rotation (+).



● HCl

RN 187793-56-2 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-[(5-aminopentyl)oxy]-4,11-diethyl-4-hydroxy-, monohydrochloride, (4S)- (9CI) (CA INDEX NAME)

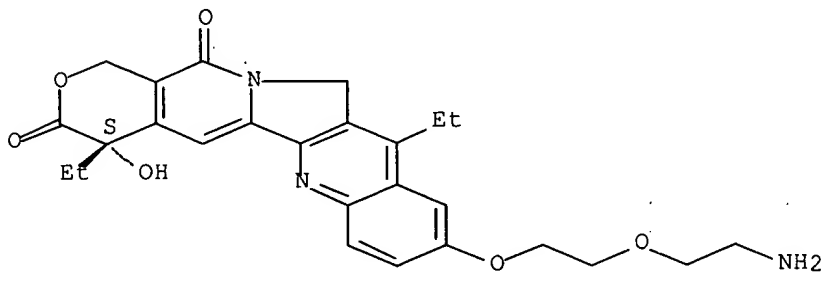
Absolute stereochemistry.



● HCl

RN 187793-58-4 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-[2-(2-aminoethoxy)ethoxy]-4,11-diethyl-4-hydroxy-, monohydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

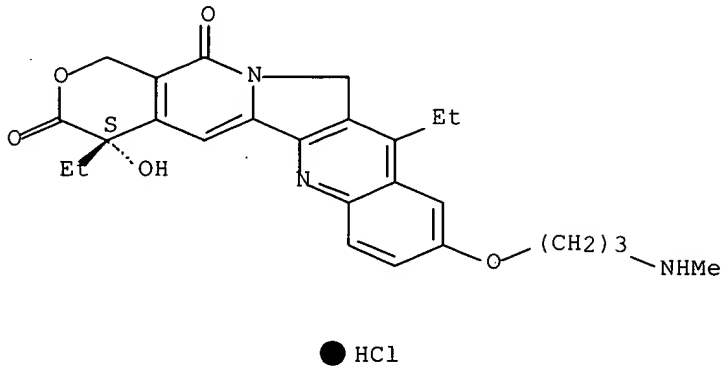


● HCl

RN 187793-60-8 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,

4,11-diethyl-4-hydroxy-9-[3-(methylamino)propoxy]-, monohydrochloride, (4S)- (9CI) (CA INDEX NAME)

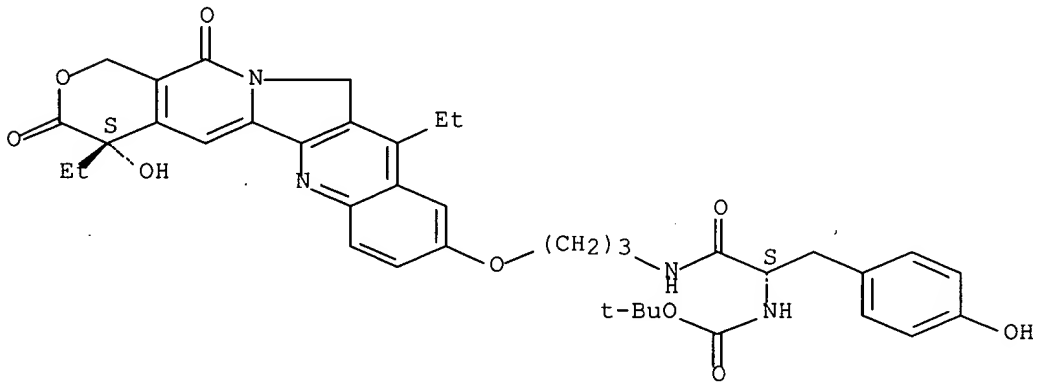
Absolute stereochemistry.



● HCl

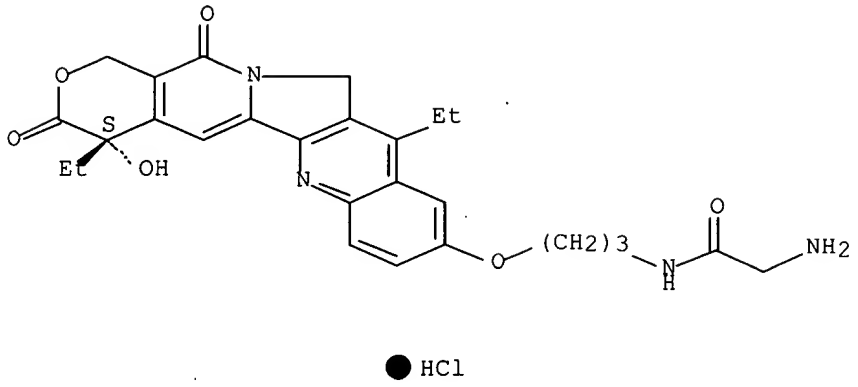
RN 187793-62-0 HCAPLUS
CN Carbamic acid, [(1S)-2-[[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]amino]-1-[(4-hydroxyphenyl)methyl]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



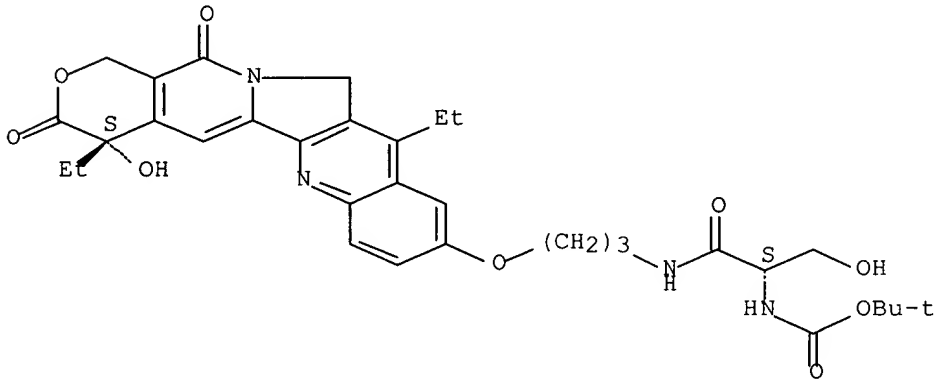
RN 187793-67-5 HCAPLUS
CN Acetamide, 2-amino-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



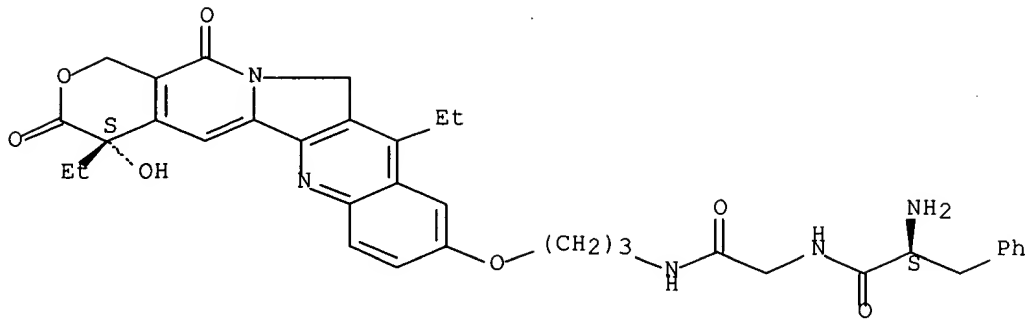
RN 187793-69-7 HCAPLUS
CN Carbamic acid, [(1S)-2-[[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]amino]-1-(hydroxymethyl)-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187793-76-6 HCAPLUS
CN Glycinamide, L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 187793-80-2 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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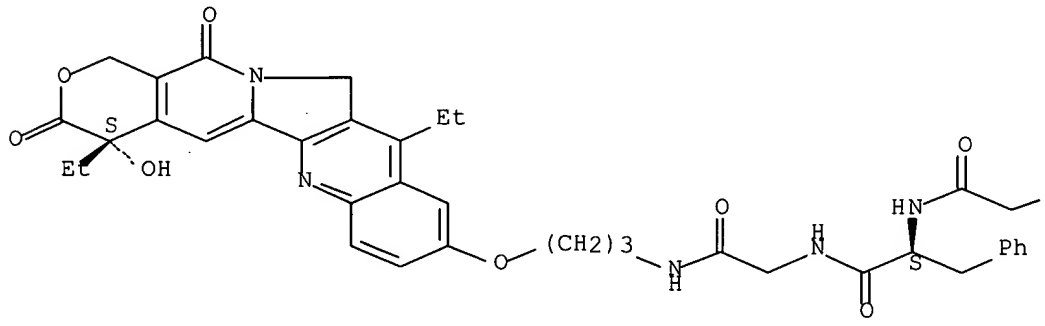

● HCl

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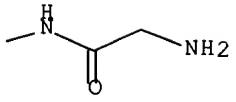

RN 187793-82-4 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[5-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]pentyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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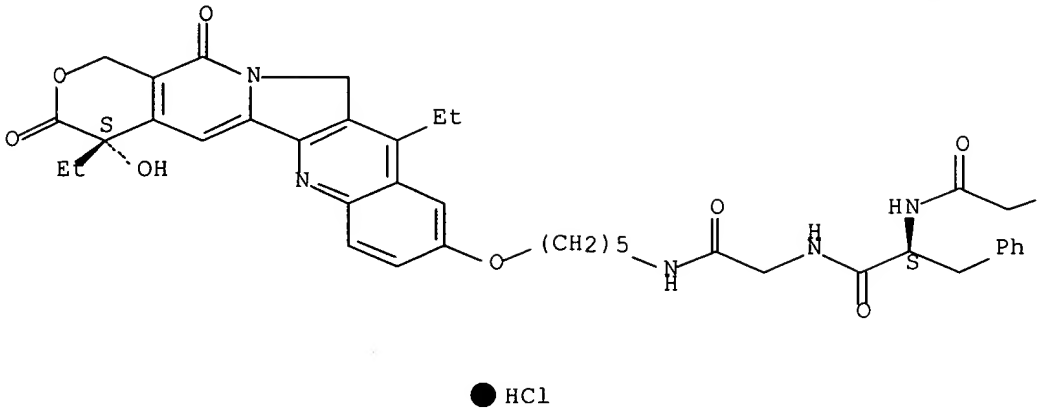

● HCl

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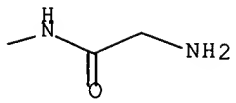

RN 187793-84-6 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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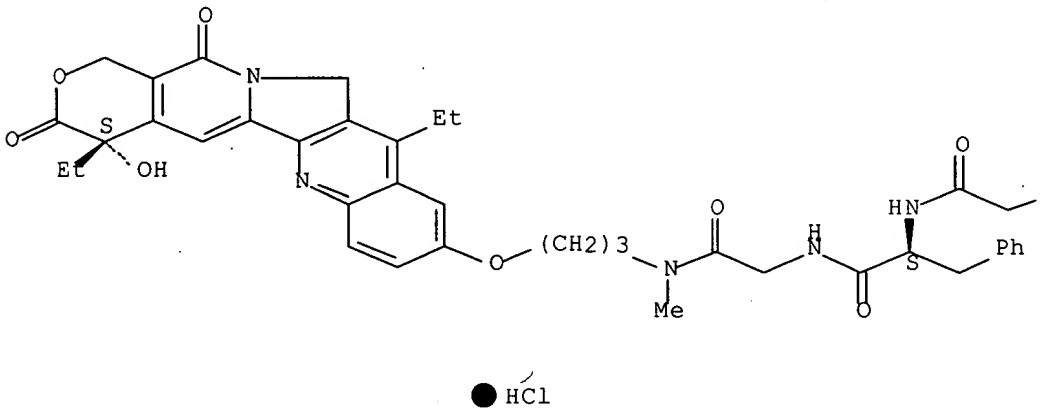

● HCl

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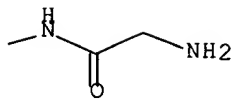

RN 187793-86-8 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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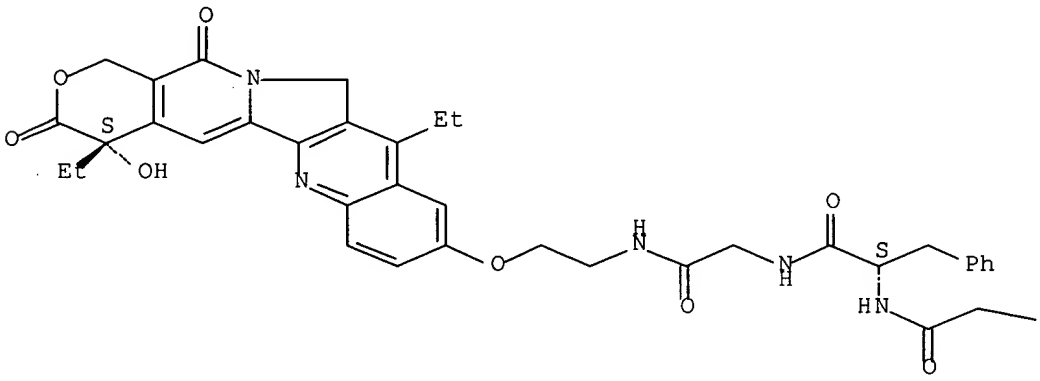

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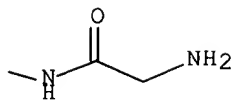
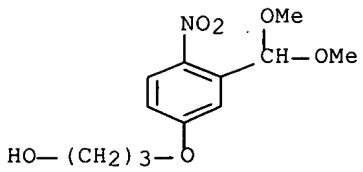
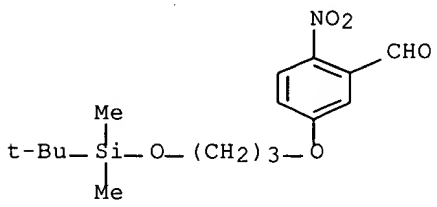
● HCl



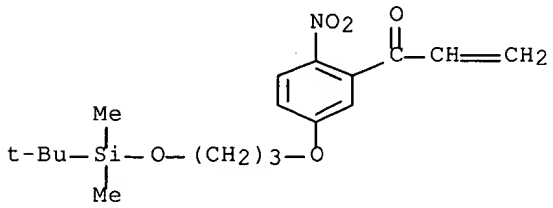
RN 187794-01-0 HCAPLUS
CN 1-Propanol, 3-[3-(dimethoxymethyl)-4-nitrophenoxy]- (9CI) (CA INDEX NAME)



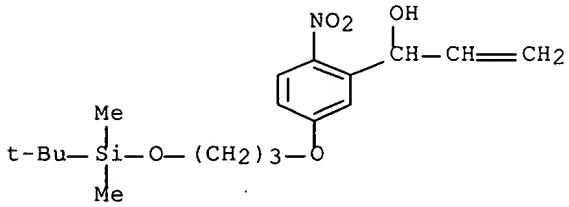
RN 187794-03-2 HCAPLUS
CN Benzaldehyde, 5-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propoxy]-2-nitro- (9CI) (CA INDEX NAME)



RN 187794-05-4 HCAPLUS
CN 2-Propen-1-one, 1-[5-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propoxy]-2-nitrophenyl]- (9CI) (CA INDEX NAME)

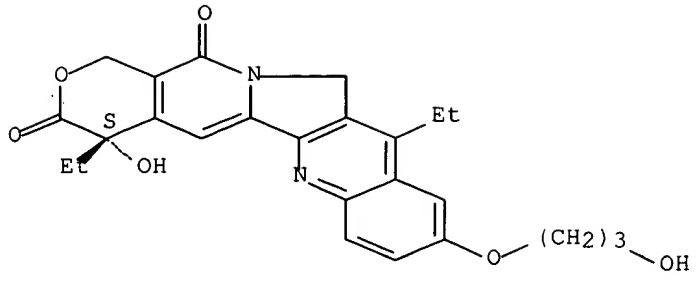


RN 187794-07-6 HCAPLUS
CN Benzenemethanol, 5-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propoxy]-.alpha.-ethenyl-2-nitro- (9CI) (CA INDEX NAME)

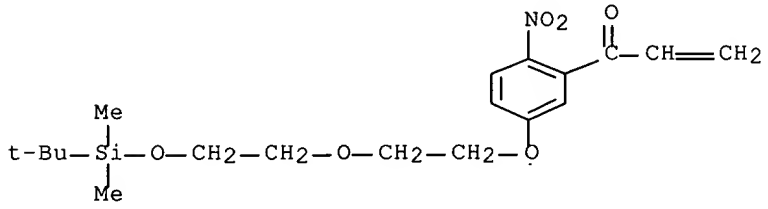


RN 187794-09-8 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4-hydroxy-9-(3-hydroxypropoxy)-, (4S)- (9CI) (CA INDEX NAME)

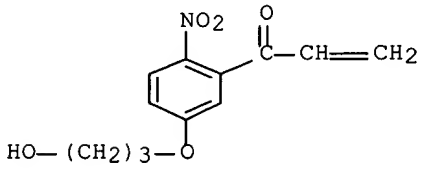
Absolute stereochemistry.



RN 187794-11-2 HCAPLUS
CN 2-Propen-1-one, 1-[5-[2-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethoxy]ethoxy]-2-nitrophenyl]- (9CI) (CA INDEX NAME)

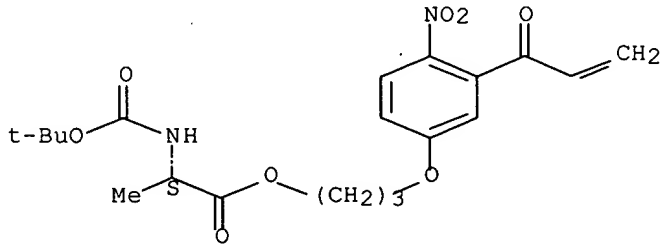


RN 187794-17-8 HCAPLUS
CN 2-Propen-1-one, 1-[5-(3-hydroxypropoxy)-2-nitrophenyl]- (9CI) (CA INDEX NAME)



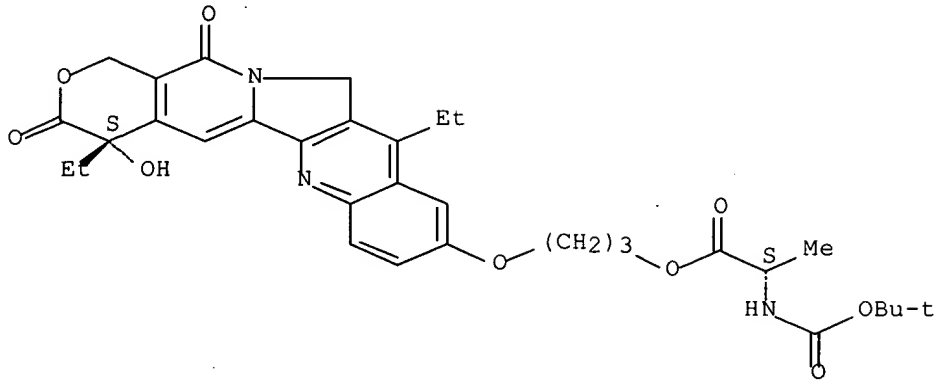
RN 187794-19-0 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 3-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



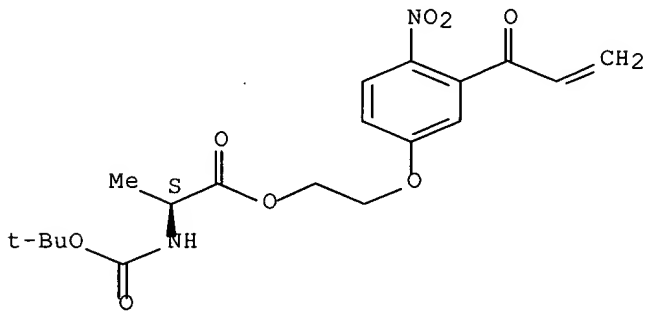
RN 187794-20-3 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



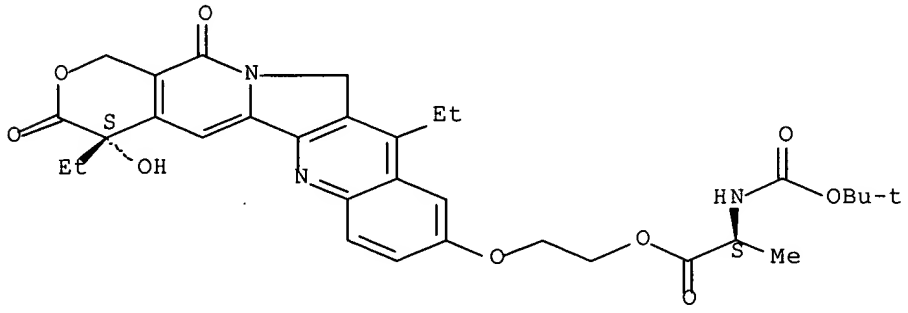
RN 187794-22-5 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 2-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



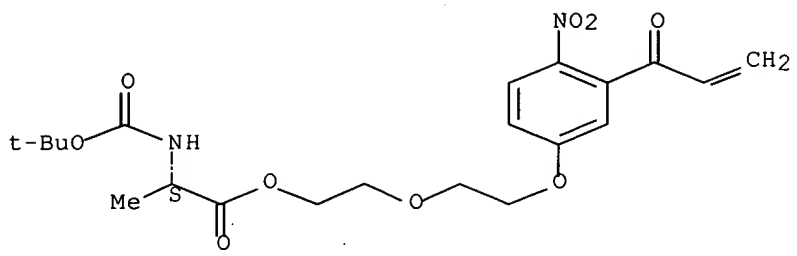
RN 187794-23-6 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187794-25-8 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 2-[2-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187794-26-9 HCAPLUS
CN L-Alanine, N-[(1,1-dimethylethoxy)carbonyl]-, 2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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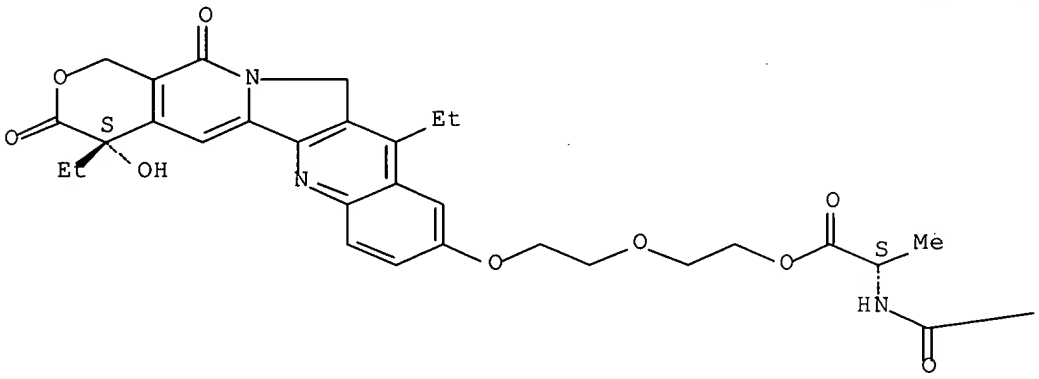

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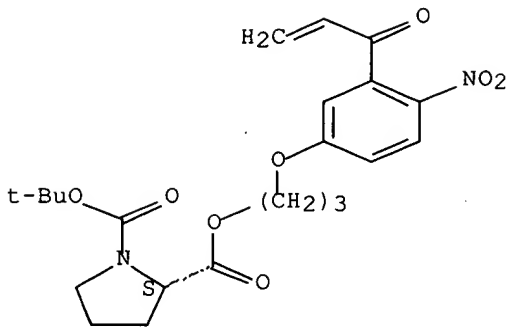
OBu-t

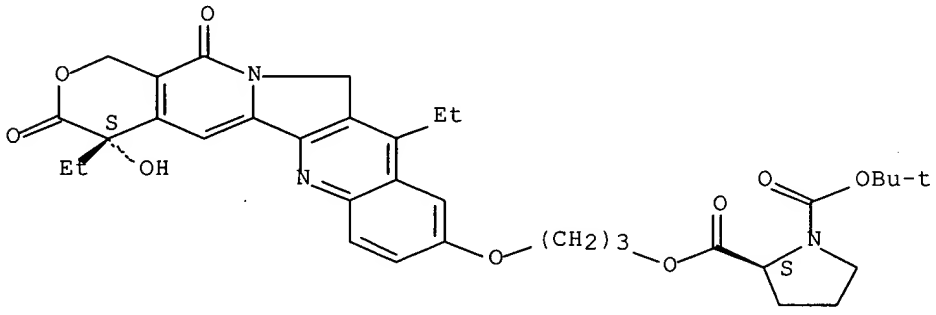
RN 187794-28-1 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 1-(1,1-dimethylethyl) 2-[3-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]propyl] ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



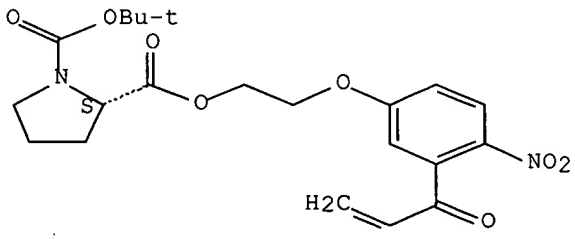
RN 187794-29-2 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 2-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl] 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



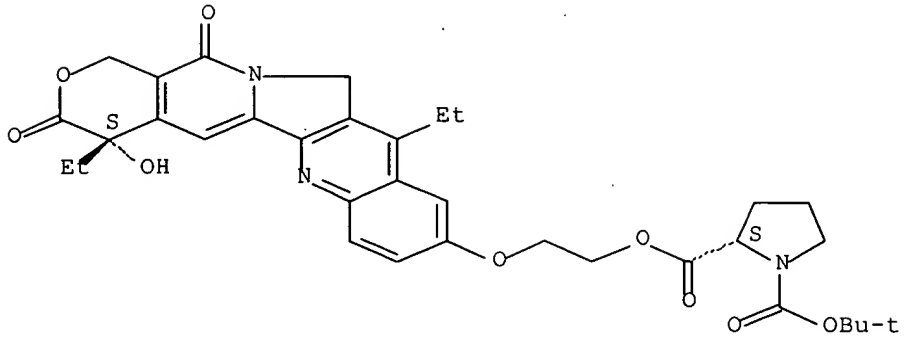
RN 187794-31-6 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 1-(1,1-dimethylethyl) 2-[2-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]ethyl] ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



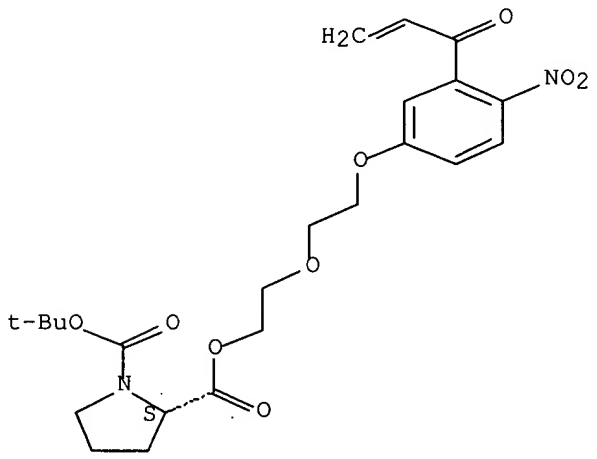
RN 187794-32-7 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl] 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187794-34-9 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 1-(1,1-dimethylethyl) 2-[2-[2-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]ethoxy]ethyl] ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187794-35-0 HCAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 2-[2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl] 1-(1,1-dimethylethyl) ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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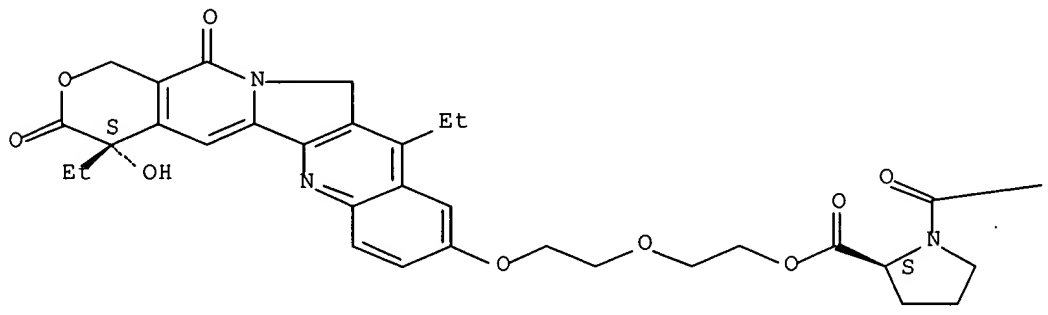

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RN 187794-47-4 HCAPLUS
CN Glycinamide, glycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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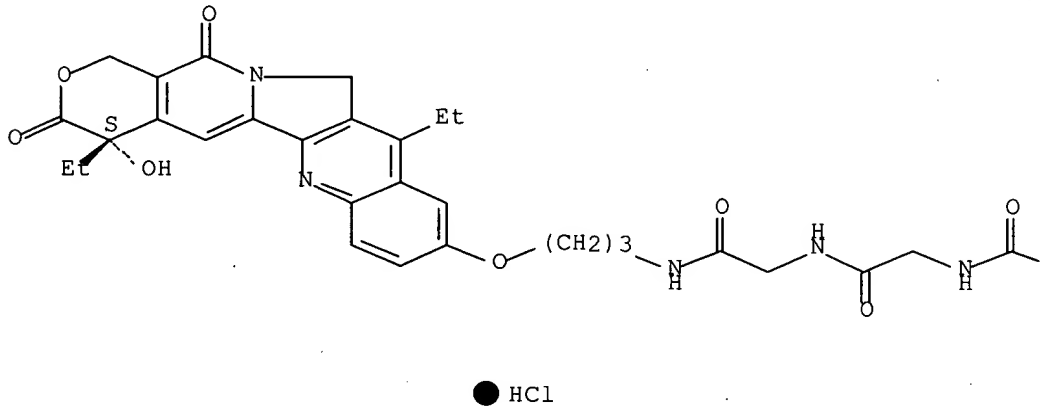

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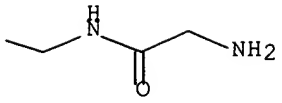

RN 187794-50-9 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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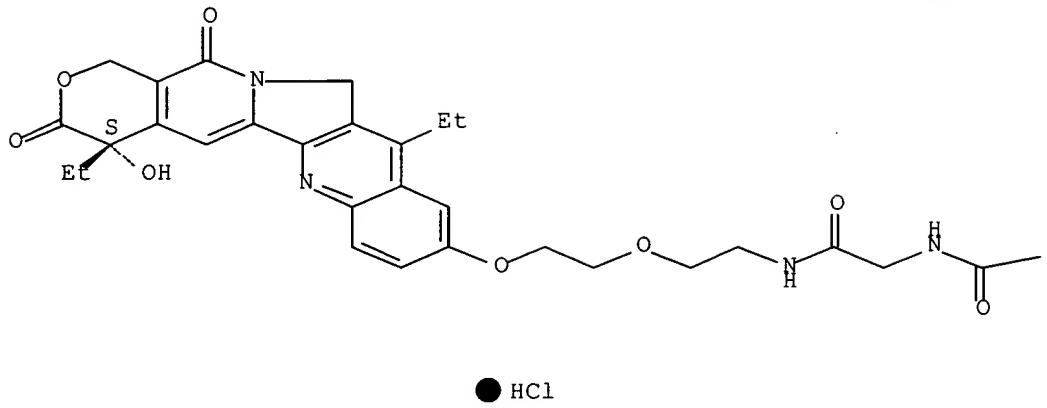

● HCl

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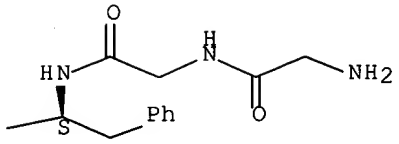

RN 187794-55-4 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl-, 3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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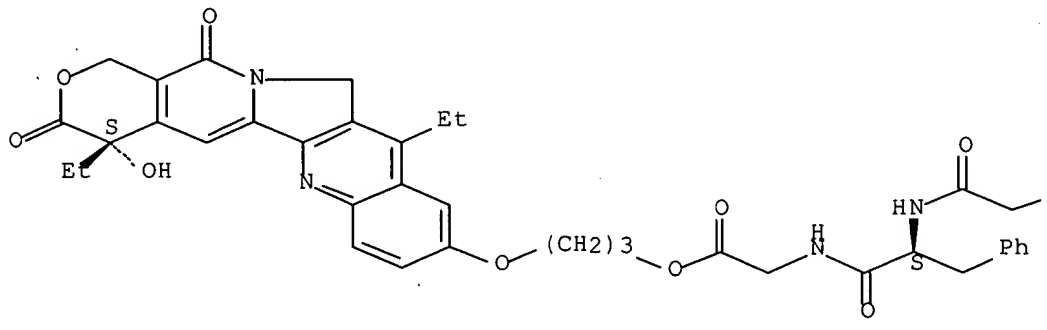

● HCl

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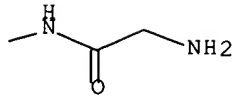
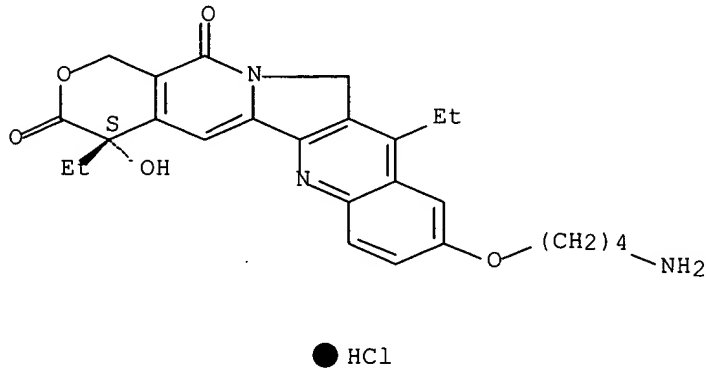


RN 187794-58-7 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 9-(4-aminobutoxy)-4,11-diethyl-4-hydroxy-, monohydrochloride, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 187794-60-1 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[4-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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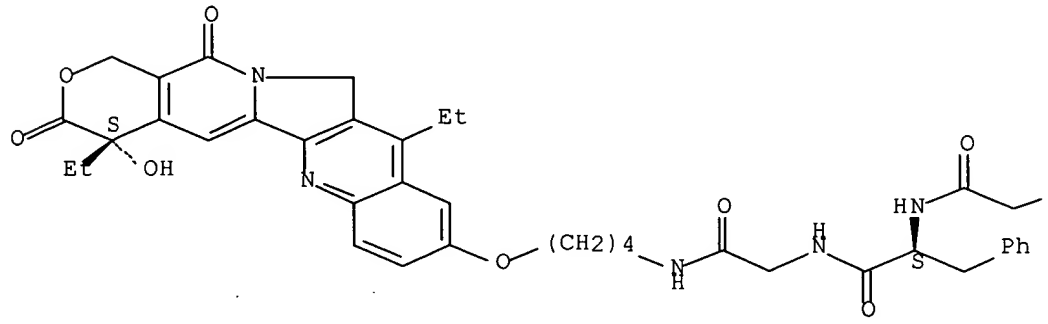
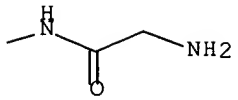
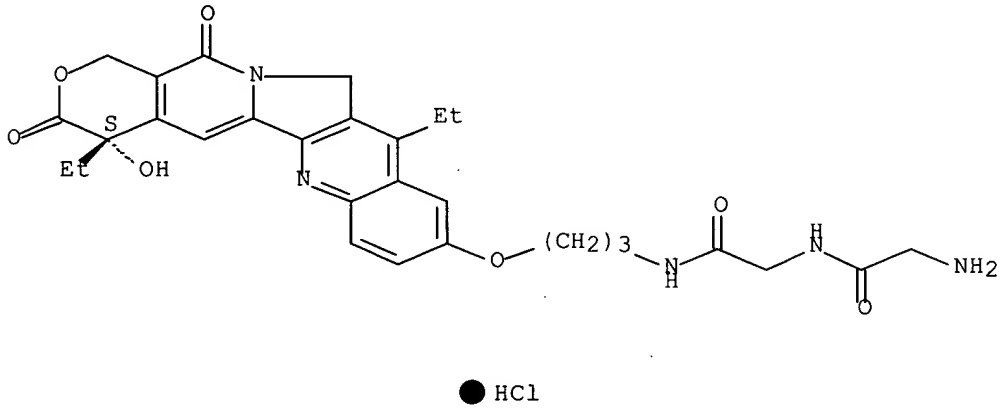


● HCl



RN 187794-66-7 HCAPLUS
CN Glycinamide, glycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

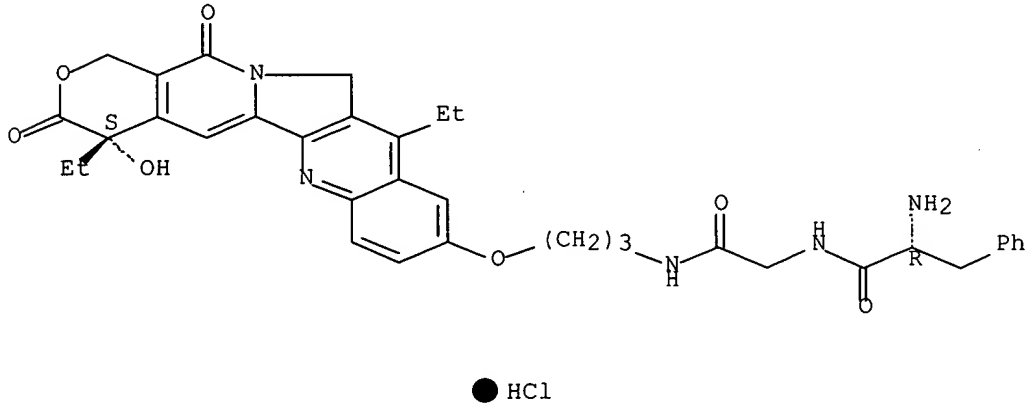
Absolute stereochemistry.



● HCl

RN 187794-68-9 HCAPLUS
CN Glycinamide, D-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 187794-70-3 HCAPLUS
CN Glycinamide, glycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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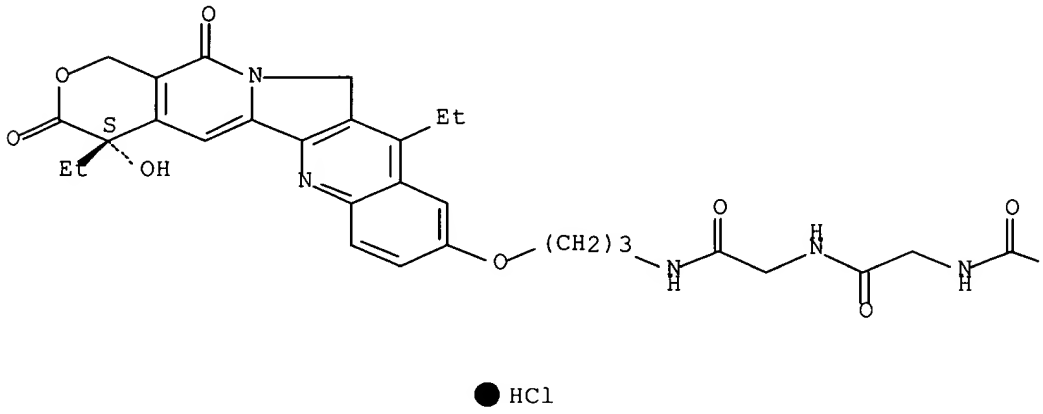

● HCl

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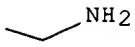

RN 187794-72-5 HCAPLUS
CN Glycinamide, glycylglycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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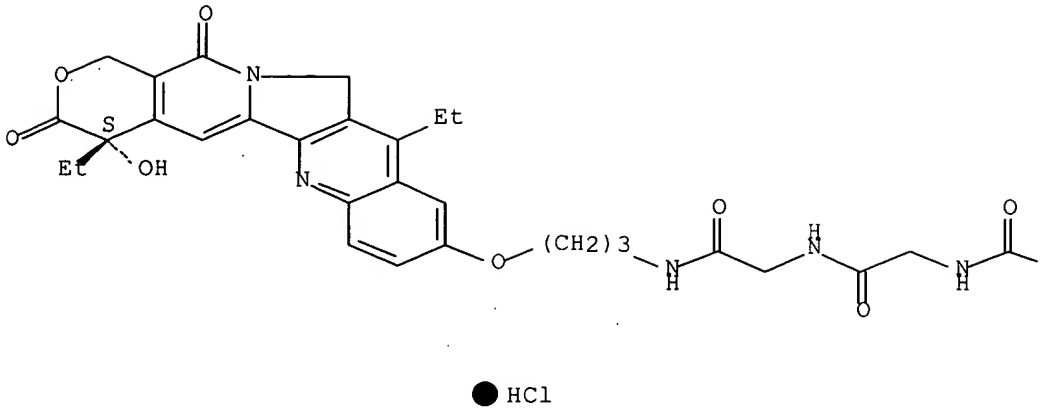

● HCl

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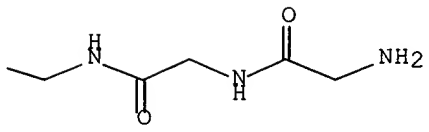

RN 187794-74-7 HCAPLUS
CN Glycinamide, glycylglycyl-D-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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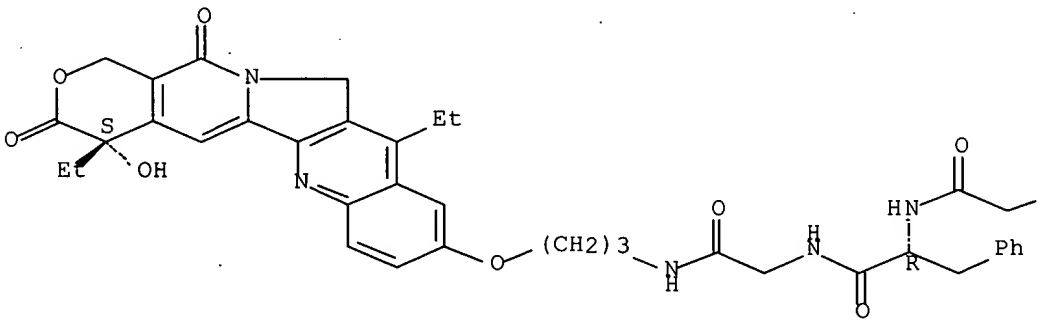
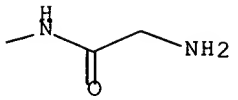
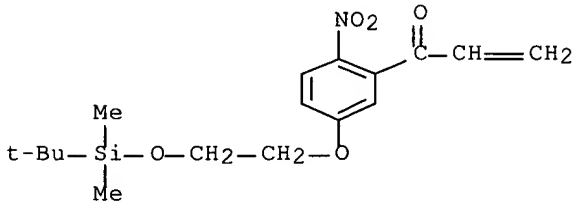


● HCl

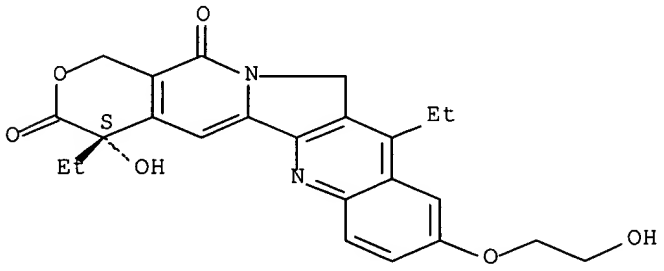


RN 187803-36-7 HCAPLUS
CN 2-Propen-1-one, 1-[5-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethoxy]-2-nitrophenyl]- (9CI) (CA INDEX NAME)

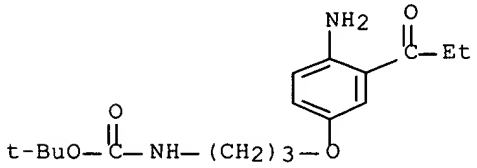


RN 187803-37-8 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,11-diethyl-4-hydroxy-9-(2-hydroxyethoxy)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 205647-87-6 HCAPLUS
CN Carbamic acid, [3-[4-amino-3-(1-oxopropyl)phenoxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 215591-99-4 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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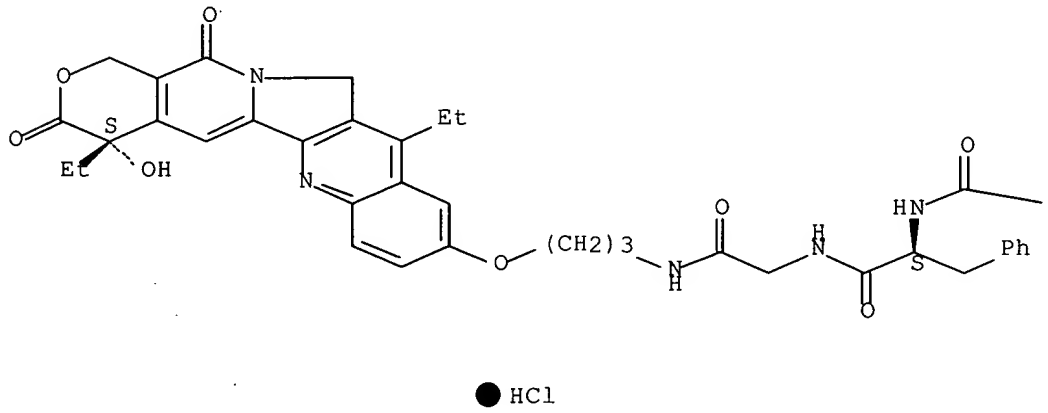

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RN 215592-00-0 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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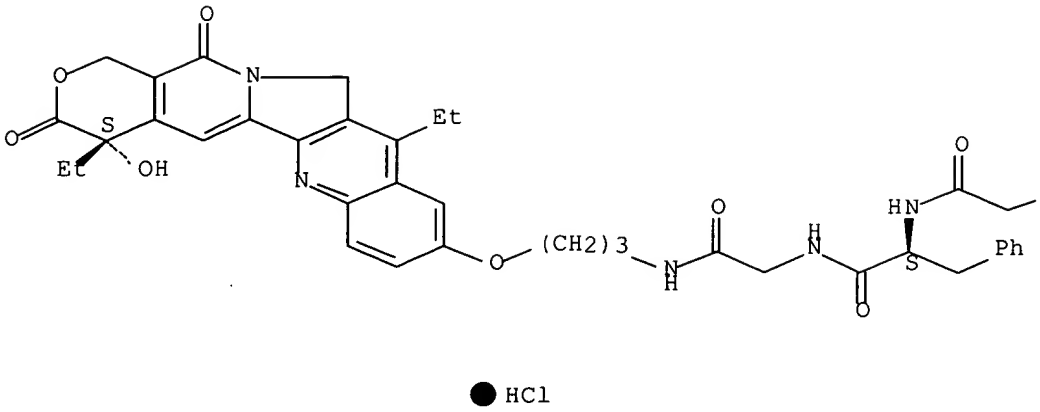

● HCl

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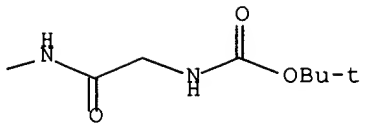
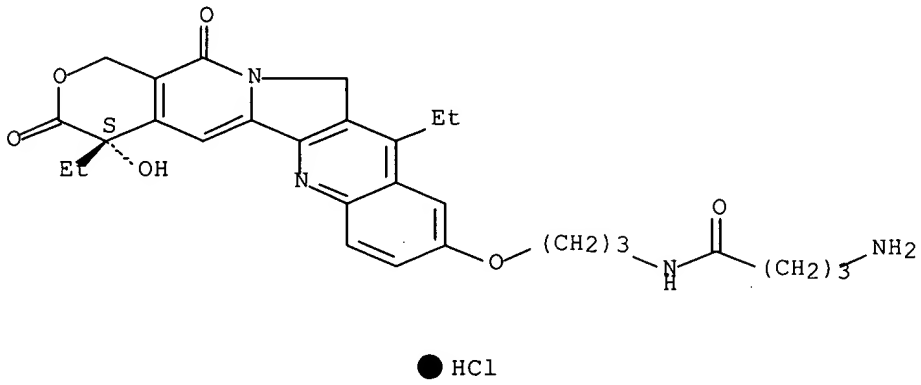


RN 215592-01-1 HCAPLUS
CN Butanamide, 4-amino-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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RN 215592-02-2 HCAPLUS
CN Butanamide, 4-[(4-amino-1-oxobutyl)amino]-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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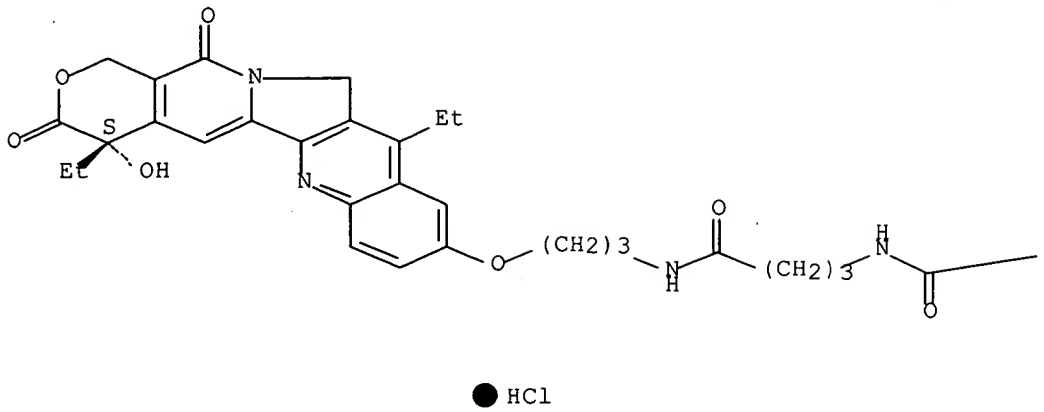

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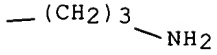
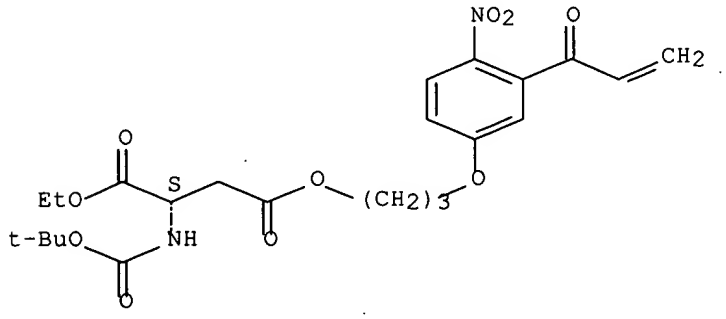


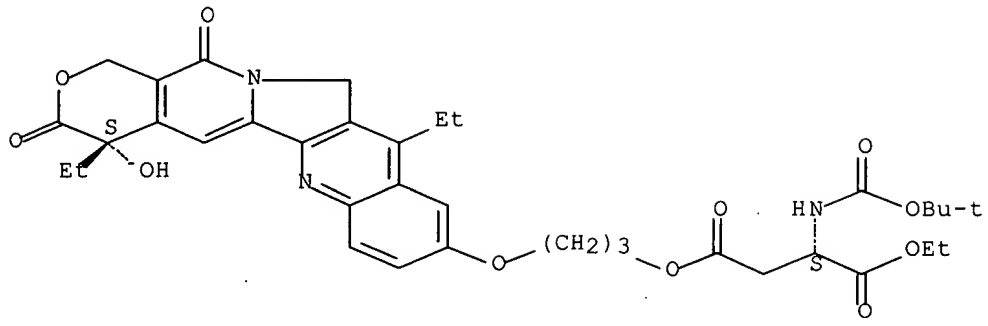
RN 215592-04-4 HCAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-ethyl 4-[3-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]propyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



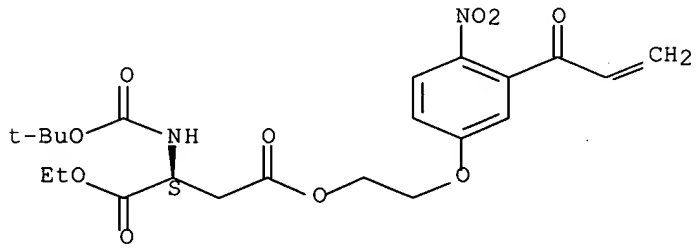
RN 215592-05-5 HCAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl] 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



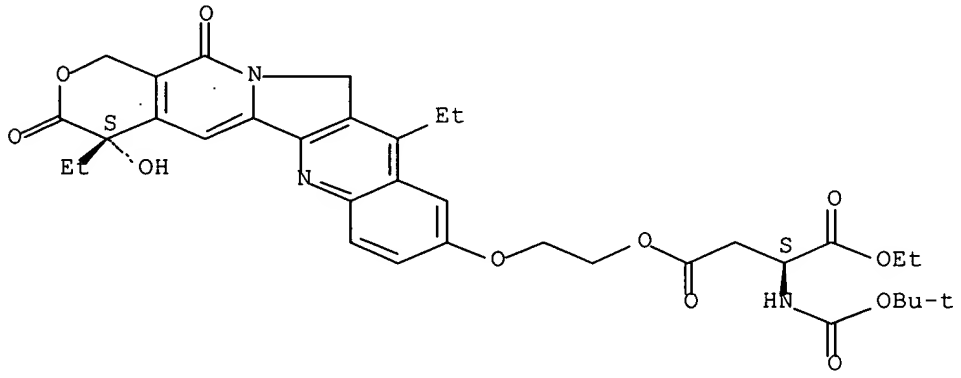
RN 215592-07-7 HCAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-ethyl 4-[2-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]ethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



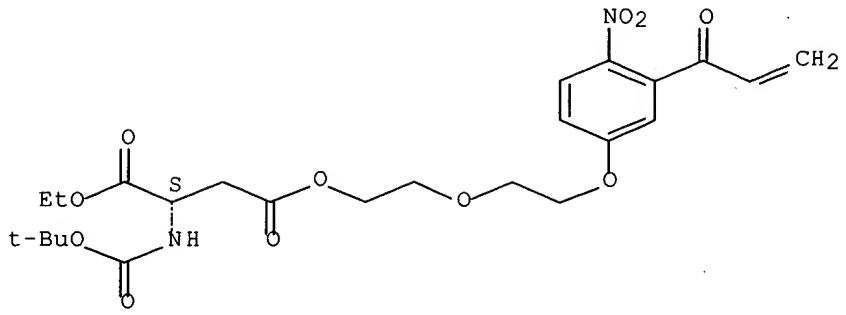
RN 215592-08-8 HCAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethyl] 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 215592-10-2 HCAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-ethyl 4-[2-[2-[4-nitro-3-(1-oxo-2-propenyl)phenoxy]ethoxy]ethyl] ester (9CI) (CA INDEX NAME)

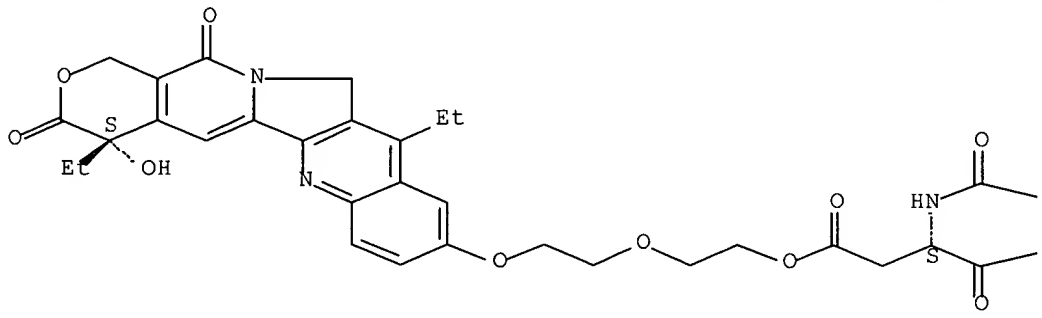
Absolute stereochemistry.



RN 215592-11-3 HCAPLUS
CN L-Aspartic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 4-[2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl] 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

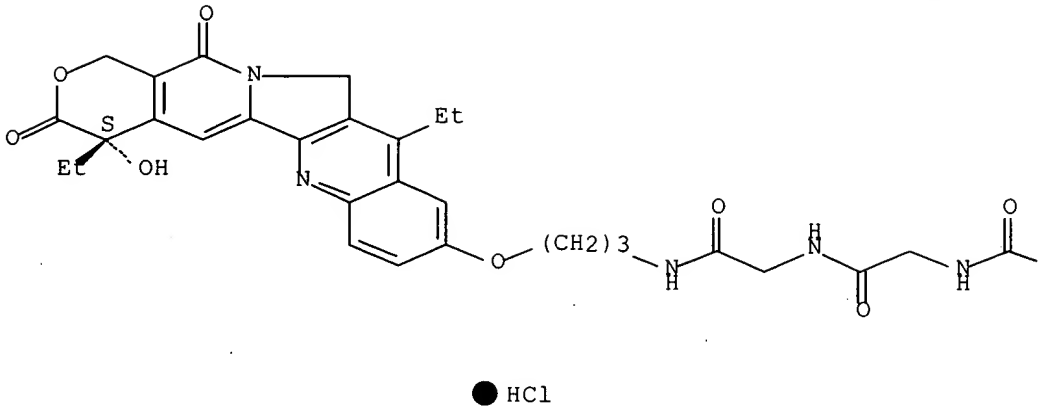
OBu-t

OEt

RN 215592-12-4 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl-N-[3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

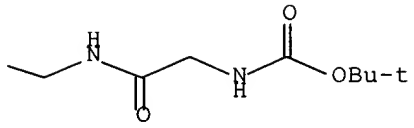
Absolute stereochemistry.

PAGE 1-A



● HCl

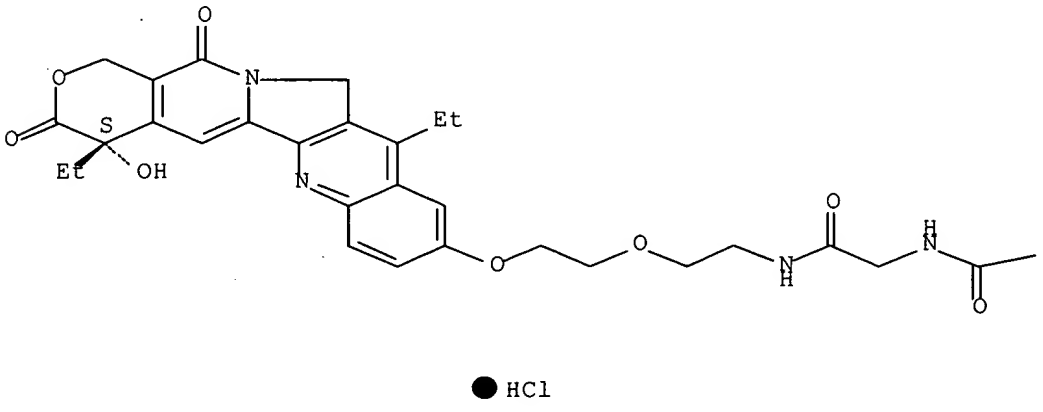
PAGE 1-B



RN 215592-13-5 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[2-[2-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]ethoxy]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

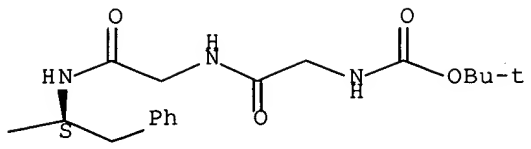
Absolute stereochemistry.

PAGE 1-A



● HCl

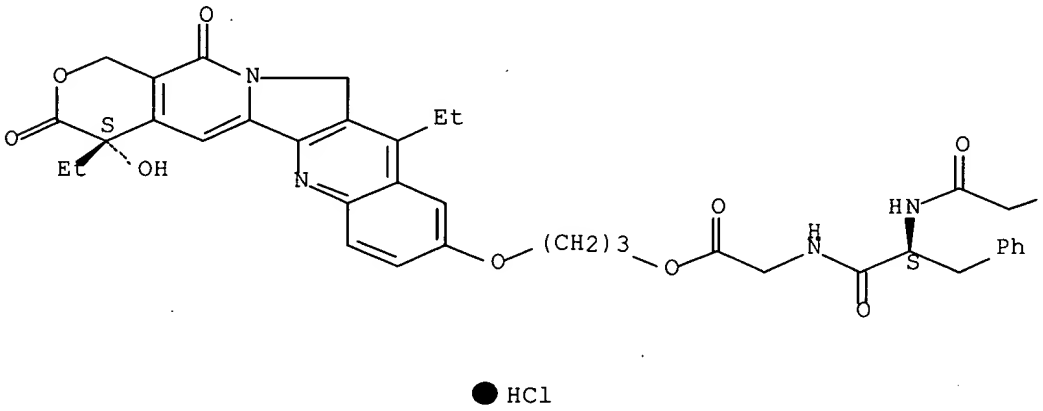
PAGE 1-B



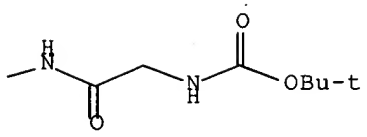
RN 215592-14-6 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-, 3-[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L47 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:127052 HCAPLUS
DOCUMENT NUMBER: 128:172026

TITLE: Extending Insulin Action in Vivo by **Conjugation** to **Carboxymethyl Dextran**

AUTHOR(S): Baudys, Miroslav; Letourneur, Didier; Liu, Feng; Mix, Don; Jozefonvicz, Jacqueline; Kim, Sung Wan

CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry/Center for Controlled Chemical Delivery, University of Utah, Salt Lake City, UT, 84112, USA

SOURCE: Bioconjugate Chemistry (1998), 9(2), 176-183
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The biochem. and pharmacol. properties of bioactive peptides and proteins can be altered by **conjugation** with polymers. This report describes site-specific attachment of insulin to activated carboxyl groups of **carboxymethyl dextran** (**CMD**, MW = 51 000) through the GlyA1 insulin amino group. On av., three or four insulin mols. were grafted to a **CMD** linear chain. Coupled insulin mols. were properly folded, and the bioactivity of **conjugated** insulin in the blood **glucose** depression assay was 9.6 IU/mg, which was only 2.6 times less than that for native insulin. The cell growth study indicated that the **CMD**-insulin **conjugate** was as mitogenic as insulin on vascular smooth muscle cells, whereas the starting **CMD** polymer was not. The insulin receptor binding const. of the **conjugate** (3.6 .times. 109 M-1) compared well with that of native insulin (7.6 .times. 109 M-1), indicating that the **CMD** chain does not present any major constraints to binding. Plasma clearance of **CMD**-insulin obeyed a two-compartment pharmacokinetic (PK) model with a **CMD**-insulin **conjugate** plasma elimination half-life of 114.1 min, which was significantly longer than that of sol. Zn-insulin (12.4 min). In contrast, pharmacodynamic (PD) profiles (blood **glucose** lowering effects) after i.v. (i.v.) administration of the **conjugate** or insulin in rats were not different. S.c. (s.c.) administration of the **conjugate** resulted in a significantly prolonged plasma profile with a noncompartmental PK parameter mean residence time (MRT) of 103.5 min which was significantly longer than that of sol. Zn-insulin (40.5 min). This was reflected in the protracted PD effect of s.c. administered **conjugate** with time needed to reach min. **glucose** concn. Tnadir of 95.7 min, which was significantly longer than that of insulin (62 min). We conclude that the **conjugation** of insulin to **CMD** leads to a bioactive **conjugate** with a delayed s.c. PD profile showing prolonged response, resembling intermediate acting insulin prepns.

IT **9004-10-8DP**, Insulin, **conjugates** with **carboxymethyl dextran**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(extending insulin action in vivo by **conjugation** to **carboxymethyl dextran**)

RN 9004-10-8 HCAPLUS

CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **9044-05-7DP**, **Carboxymethyl dextran**, **conjugates** with insulin
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);

PREP (Preparation); PROC (Process); USES (Uses)
(extending insulin action in vivo by **conjugation** to **carboxymethyl dextran**)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

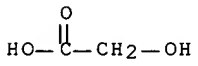
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



L47 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:777835 HCAPLUS
DOCUMENT NUMBER: 128:97464
TITLE: Design of macromolecular biological response modifier by immobilizing of D-glucose analog of muramyl dipeptide on carboxymethyl-dextran having mannose branches
AUTHOR(S): Murata, J.; Nagae, H.; Ohya, Y.; Ouchi, T.
CORPORATE SOURCE: Dep. Applied Chem., Faculty Eng., Kansai Univ., Suita, 564, Japan
SOURCE: Journal of Biomaterials Science, Polymer Edition (1997), 8(12), 931-946
CODEN: JBSEEA; ISSN: 0920-5063
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It is well known that muramyl dipeptide is a min. required structure of bacterial peptidoglycan responsible for immunoadjuvant activity. Since mannose receptors exists on the surface of macrophages, polymers with branched mannose residues are expected to target moieties to macrophages. To achieve an efficient delivery of D-**glucose** analog of muramyl dipeptide (GADP) via receptor-mediated endocytosis by mannose receptors on the surface of macrophages, GADP/**carboxymethyl-dextran** (CM-Dex)/Man **conjugate** was synthesized. Moreover, to study the effect of the introduction of mannose residues, we also synthesized GADP/CM-glucomannan (CM-GM) and GADP/CM-Dex **conjugates**. The immunol. enhancement activities of their **conjugates** were evaluated by measurements of **glucose** consumption and .beta.-D-glucuronidase activity from macrophage-like cells. The GADP/CM-Dex/Man and GADP/CM-GM **conjugates** showed higher immunol. enhancement activity than the GADP/CM-Dex **conjugate**. The immunol. enhancement activity of GADKP/CM-Dex/Man and GADP/CM-GM **conjugates** was decreased to the same level of immunol enhancement activity of GADP/CM-Dex **conjugate** under the presence of excess mannose. These results suggested that the introduction of mannose

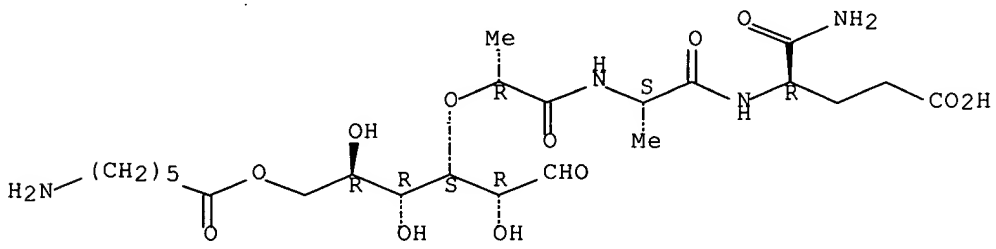
residues into GADP/CM-Dex **conjugate** could increase the affinity against macrophage and the immunol. enhancement activity of GADP/CM-Dex **conjugate** itself.

IT **146916-64-5DP**, reaction products with CM-dextran or CM-glucomannan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design of macromol. biol. response modifier by immobilizing glucose analog of muramyl dipeptide on CM-dextran having mannose branches)

RN 146916-64-5 HCAPLUS

CN D-.alpha.-Glutamine, N-[(2R)-2-[6-O-(6-amino-1-oxohexyl)-D-glucos-3-O-yl]-1-oxopropyl]-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

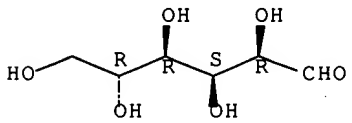


IT **50-99-7**, D-Glucose, reactions **617-04-9**, Methyl .alpha.-D-mannopyranoside **6404-29-1 9044-05-7D**, Carboxymethyl dextran, reaction products with glucose analog of muramyldipeptide **9064-52-2D**, Carboxymethyl glucomannan, reaction products with glucose analog of muramyldipeptide **77987-49-6**, N-Benzyloxycarbonylethanolamine **107947-55-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(design of macromol. biol. response modifier by immobilizing glucose analog of muramyl dipeptide on CM-dextran having mannose branches)

RN 50-99-7 HCAPLUS

CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

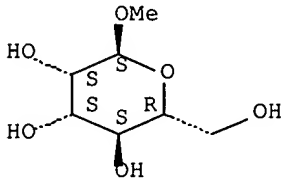
Absolute stereochemistry.



RN 617-04-9 HCAPLUS

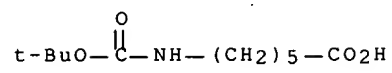
CN .alpha.-D-Mannopyranoside, methyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 6404-29-1 HCAPLUS

CN Hexanoic acid, 6-[[(1,1-dimethylethoxy)carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

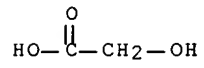
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9064-52-2 HCAPLUS
CN D-Gluco-D-mannan, carboxymethyl ether (9CI) (CA INDEX NAME)

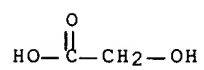
CM 1

CRN 11078-31-2
CMF Unspecified
CCI PMS, MAN

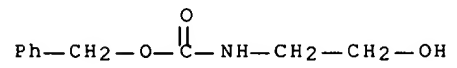
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3

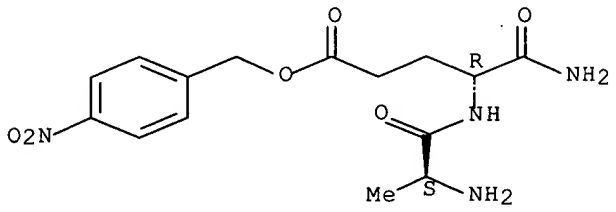


RN 77987-49-6 HCAPLUS
CN Carbamic acid, (2-hydroxyethyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 107947-55-7 HCAPLUS
CN D-.alpha.-Glutamine, L-alanyl-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

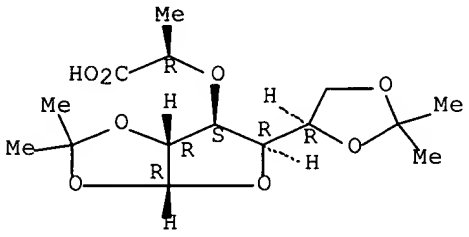
Absolute stereochemistry.



IT **74112-33-7P 78609-16-2P**, .alpha.-D-Mannopyranose, 2,3,4,6-tetrakis-O-(phenylmethyl)- **92470-93-4P**, 2,3,4,6-Tetra-O-benzyl-.alpha.-D-mannopyranosyl chloride **140428-88-2DP**, reaction products with CM-dextran and glucose analog of muramyldipeptide **140428-88-2P 146916-64-5P 201145-84-8P 201145-85-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design of macromol. biol. response modifier by immobilizing glucose analog of muramyl dipeptide on CM-dextran having mannose branches)

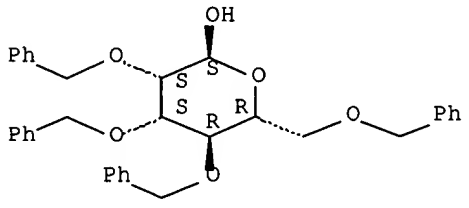
RN 74112-33-7 HCAPLUS
CN .alpha.-D-Glucofuranose, 3-O-(1-carboxyethyl)-1,2:5,6-bis-O-(1-methylethylidene)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 78609-16-2 HCAPLUS
CN .alpha.-D-Mannopyranose, 2,3,4,6-tetrakis-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

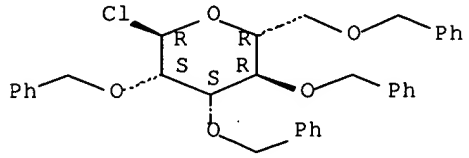
Absolute stereochemistry. Rotation (+).



RN 92470-93-4 HCAPLUS
CN .alpha.-D-Mannopyranosyl chloride, 2,3,4,6-tetrakis-O-(phenylmethyl)-

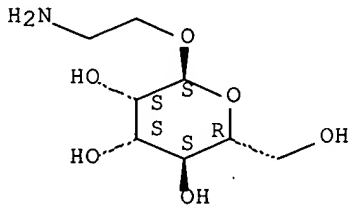
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



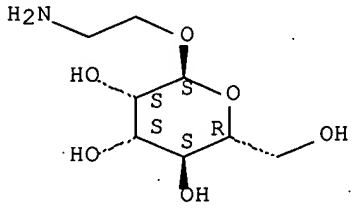
RN 140428-88-2 HCAPLUS.
CN .alpha.-D-Mannopyranoside, 2-aminoethyl (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



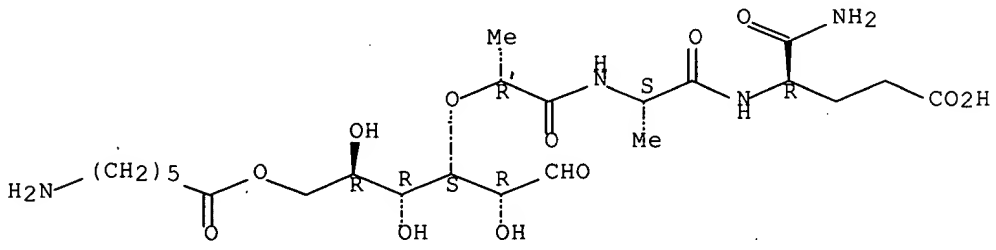
RN 140428-88-2 HCAPLUS
CN .alpha.-D-Mannopyranoside, 2-aminoethyl (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



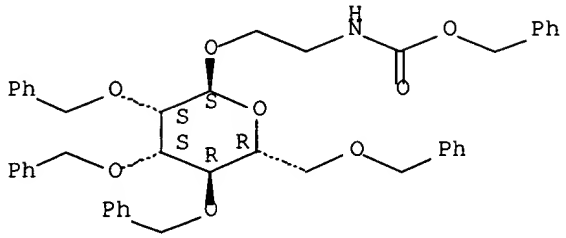
RN 146916-64-5 HCAPLUS
CN D-.alpha.-Glutamine, N-[(2R)-2-[6-O-(6-amino-1-oxohexyl)-D-glucos-3-O-yl]-1-oxopropyl]-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



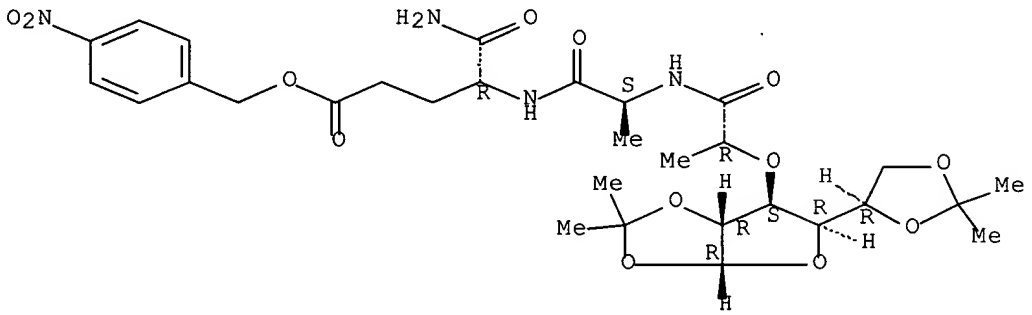
RN 201145-84-8 HCAPLUS
CN Carbamic acid, [2-[[2,3,4,6-tetrakis-O-(phenylmethyl)-.alpha.-D-mannopyranosyl]oxy]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 201145-85-9 HCAPLUS
CN D-.alpha.-Glutamine, N-[(2R)-2-[1,2:5,6-bis-O-(1-methylethylidene)-.alpha.-D-glucofuranos-3-O-yl]-1-oxopropyl]-L-alanyl-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

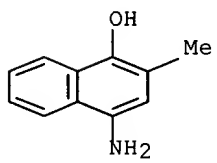


L47 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:138228 HCAPLUS
DOCUMENT NUMBER: 126:242714
TITLE: Targeted delivery of drugs and proteins to the liver via receptor-mediated endocytosis
AUTHOR(S): Hashida, Mitsuru; Hirabayashi, Hideki; Nishikawa, Makiya; Takakura, Yoshinobu
CORPORATE SOURCE: Department of Drug Delivery Research, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, Japan
SOURCE: J. Controlled Release (1997), 46(1,2), 129-137
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Targeting of drugs and proteins to the liver via the asialoglycoprotein receptor was investigated in mice. **Carboxymethyl-dextran** (**CMD**), carboxymethyl-amylose (CMA), and poly-L-glutamic acid (PLGA) were modified with 2-imino-2-methoxyethyl (IME)-thiogalactosides to obtain galactosylated derivs. as carriers of drugs with low-mol. wts. Proteins were targeted to the liver by direct attachment of **galactose** moieties. Pharmacokinetic anal. clearly showed that galactosylated derivs. were taken up by the liver depending on the mol. wt. and configuration of macromols., the no. of **galactose** residues, and the administered dose. Based on the obtained results, we attempted to selectively deliver vitamin K5, which acts as a coagulant in

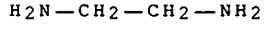
the liver. Galactosylated PLGA (Gal-PLGA) possessing 18 **galactose** residues was selected as a hepatotropic carrier since it was efficiently accumulated and gradually degraded in the liver after i.v. injection. The attachment of vitamin K5 did not alter the distribution properties of Gal-PLGA, and vitamin K5 was successfully delivered to the liver by the **conjugation**. The anti-hemorrhagic activity of the **conjugate** was assayed after i.v. injection in mice treated with warfarin. Vitamin K5 **conjugated** with Gal-PLGA showed coagulant activity at any periods studied after i.v. injection, while free vitamin K5 only showed the activity at 4 h after administration. These results indicate the usefulness of galactosylated macromols. as hepatotropic carriers of drugs whose site of action is in the liver.

IT **83-70-5D**, Vitamin K5, reaction products with galactosylated poly(glutamic acid) **107-15-3D**, 1,2-Ethanediamine, reaction products with polysaccharides and galactose deriv. **9044-05-7D**, Carboxymethyl dextran, glycosylated **9054-89-1D**, Superoxide dismutase, galactosylated **12768-31-9D**, Carboxymethyl amylose, glycosylated **24991-23-9D**, glycosylated **25513-46-6D**, Poly(L-glutamic acid), glycosylated **75204-21-6D**, reaction products with macromols.
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(targeted delivery of drugs and proteins to the liver via receptor-mediated endocytosis)

RN 83-70-5 HCAPLUS
CN 1-Naphthalenol, 4-amino-2-methyl- (9CI) (CA INDEX NAME)



RN 107-15-3 HCAPLUS
CN 1,2-Ethanediamine (9CI) (CA INDEX NAME)



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

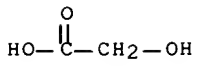
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 12768-31-9 HCAPLUS
CN Amylose, carboxymethyl ether (9CI) (CA INDEX NAME)

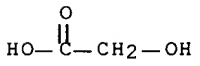
CM 1

CRN 9005-82-7
CMF Unspecified
CCI PMS, MAN

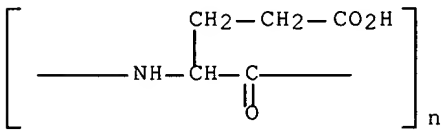
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 24991-23-9 HCAPLUS
CN Poly[imino[(1S)-1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)

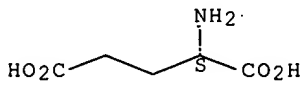


RN 25513-46-6 HCAPLUS
CN L-Glutamic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 56-86-0
CMF C5 H9 N O4
CDES 5:L

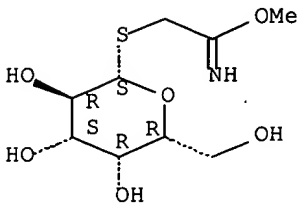
Absolute stereochemistry.



RN 75204-21-6 HCAPLUS
CN Ethanimidic acid, 2-(.beta.-D-galactopyranosylthio)-, methyl ester (9CI)

(CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:524125 HCAPLUS
DOCUMENT NUMBER: 125:219918
TITLE: Role of the **Polysaccharide** Content and Net Charge on the Emulsifying Properties of .beta.-Lactoglobulin-Carboxymethyldextran **Conjugates**
AUTHOR(S): Nagasawa, Koichi; Ohgata, Koki; Takahashi, Koji; Hattori, Makoto
CORPORATE SOURCE: Faculty of Agriculture, Tokyo University of Agriculture and Technology, Tokyo, 183, Japan
SOURCE: J. Agric. Food Chem. (1996), 44(9), 2538-2543
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .beta.-Lactoglobulin (.beta.-LG)-carboxymethyldextran (**CMD**) **conjugates** were prepd. by using water-sol. carbodiimide. Three kinds of **CMD** differing in mol. mass (40, 70, and 162 kDa) were used to investigate the effects of different **CMD** contents and net charge on the functional changes in .beta.-LG. The emulsifying properties of these .beta.-LG-**CMD conjugates** were investigated under various conditions by evaluating the stability of oil/water emulsions prepd. with oleic acid and the .beta.-LG-**CMD conjugates**. The emulsifying ability of .beta.-LG was greatly improved by **conjugating** with **CMD** in the acidic pH range in the presence of less than 0.5 M NaCl. After heating at 80 .degree.C for 10 min, the emulsifying stability of the .beta.-LG-**CMD conjugates** was higher than that of .beta.-LG. It is thought that increasing the **polysaccharide** content and shifting the isoelec. point of .beta.-LG to the acidic side by **conjugating** with **CMD** of a high mol. wt. would be effective in improving the emulsifying properties of .beta.-LG under unfavorable conditions.

IT **7647-14-5**, Sodium chloride, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**polysaccharide** content and net charge effect on emulsifying properties of .beta.-lactoglobulin-carboxymethyldextran **conjugates**)
RN 7647-14-5 HCAPLUS
CN Sodium chloride (NaCl) (9CI) (CA INDEX NAME)

Cl—Na

IT **9044-05-7D**, Carboxymethyldextran, **conjugates** with .beta.-lactoglobulin
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(**polysaccharide** content and net charge effect on emulsifying properties of .beta.-lactoglobulin-carboxymethyldextran **conjugates**)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

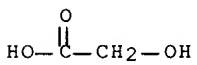
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



L47 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:507742 HCAPLUS
DOCUMENT NUMBER: 125:204231
TITLE: Pharmacokinetics and targeted delivery of proteins and genes
AUTHOR(S): Hashida, Mitsuru; Mahato, Ram I.; Kawabata, Kenji; Miyao, Takenori; Nishikawa, Makiya; Takakura, Yoshinobu
CORPORATE SOURCE: Fac. Pharmaceutical Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: J. Controlled Release (1996), 41(1,2, Fifth International Symposium on Delivery and Targeting of Pesticides, Proteins and Genes, 1995), 91-97
CODEN: JCREEC; ISSN: 0168-3659
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effectiveness of various approaches for controlling in vivo disposition of proteins and genes is compared based on pharmacokinetic anal. The potential of introduction of **galactose** or mannose residues aiming at receptor-mediated endocytosis, succinylation to be recognized by a scavenger receptor, and cationization for universal electrostatic interaction were characterized using model proteins. Corresponding to the results, a superior therapeutic effect was shown with derivs. of superoxide dismutase against hepatic and renal ischemia/reperfusion injury. A similar approach was adopted for plasmid DNA and oligonucleotide and their rapid degrdn. in the blood pool and preferential uptake by the liver after i.v. injection were characterized by pharmacokinetic anal. The effects of incorporation into cationic liposomes and **conjugation** with macromols. on their in vivo distribution were also elucidated.
IT **9044-05-7DP**, Carboxymethyldextran, conjugates with 5'-biotinylated

decathymidylic acid **167497-81-6DP, conjugates** with **carboxymethyl dextran**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(pharmacokinetics and targeted delivery of proteins and genes)

RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

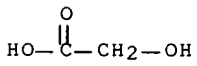
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

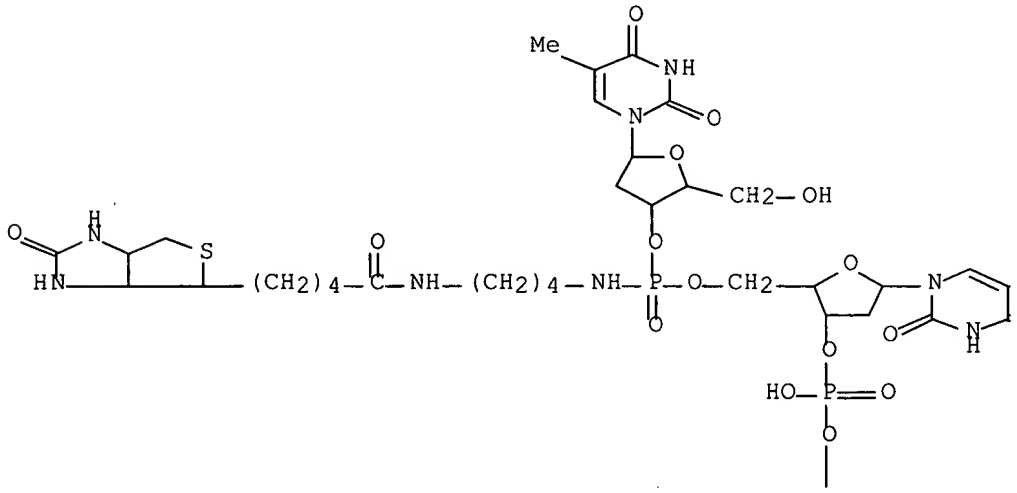
CM 2

CRN 79-14-1
CMF C2 H4 O3

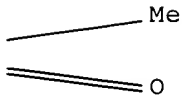


RN 167497-81-6 HCAPLUS
CN Thymidine, P-deoxy-P-[[4-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]butyl]amino]thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-thymidylyl-(3'.fwdarw.5')-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]- (9CI) (CA INDEX NAME)

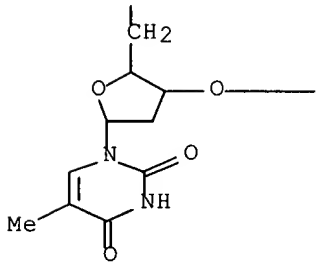
PAGE 1-A



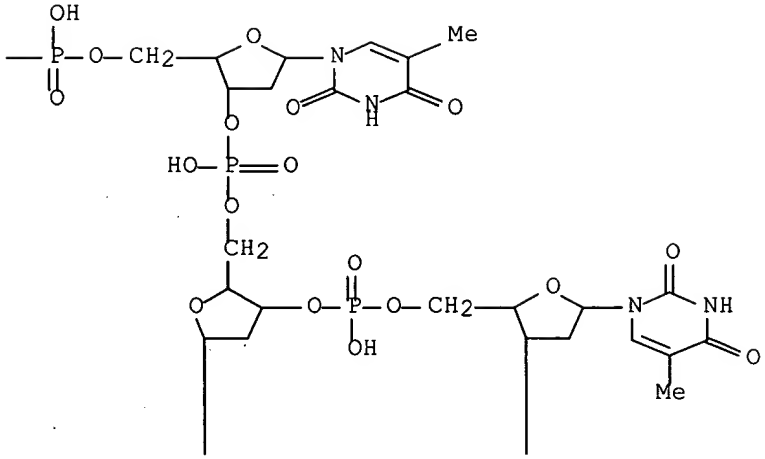
PAGE 1-B



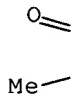
PAGE 2-A



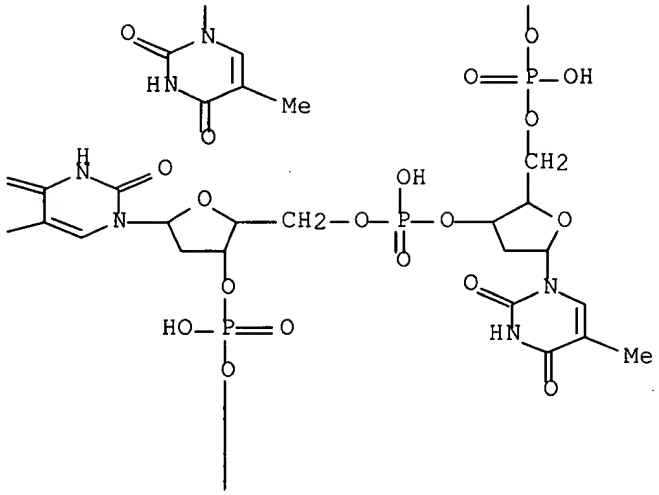
PAGE 2-B



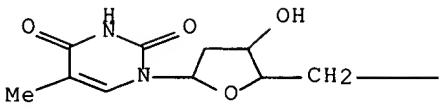
PAGE 3-A



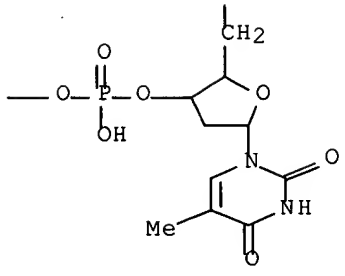
PAGE 3-B



PAGE 4-A



PAGE 4-B



IT **9001-63-2**, Lysozyme **9035-81-8**, Trypsin inhibitor
9054-89-1, Superoxide dismutase

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics and targeted delivery of proteins and genes)
RN 9001-63-2 HCAPLUS
CN Lysozyme (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9035-81-8 HCAPLUS
CN Trypsin inhibitor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L47 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:478465 HCAPLUS
DOCUMENT NUMBER: 125:204200
TITLE: Synthesis of muramyl dipeptide analog-glucomannan conjugate and its stimulation activity against macrophage-like cells
AUTHOR(S): Murata, Jun-ichi; Nagae, Hiromu; Ohya, Yuichi; Ouchi, Tatsuro
CORPORATE SOURCE: Department of Applied Chemistry, Kansai University, Suita, 564, Japan
SOURCE: Carbohydr. Polym. (1996), 29(2), 111-118
CODEN: CAPOD8; ISSN: 0144-8617
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Since the mannose receptors exist on the surface of macrophages, the branched mannose residues of glucomannan are expected to act as targeting moieties to macrophages. So, to achieve an efficient delivery of D-**glucose** analog of muramyl dipeptide (GADP) via receptor-mediated endocytosis by mannose receptors on the surface of macrophages, the GADP/carboxymethyl(CM)-glucomannan **conjugate** was synthesized. Moreover, to study the relation between the immunol. enhancement activity of the **conjugates** and their mannose residues, we synthesized the GADP/CM-glucomannan **conjugates** having various degrees of substitution of carboxymethyl group in mol% per sugar unit (DCM) and GADP/CM-dextran **conjugate** through hybridization of GADP with dextran. The immunol. enhancement activities of GADP/CM-glucomannan **conjugates** and GADP/CM-dextran **conjugate** were evaluated by measurements of the **glucose** consumption, the superoxide anion prodn. and the .beta.-D-glucuronidase activity from PMA (phorbol-12-myristate-13-acetate)-differentiated HL-60 (human promyelocytic leukemia) or U937 (human monoblast leukemia) cells as macrophage-like cells.
IT **9044-05-7DP, Carboxymethyl dextran,**
conjugates with **glucose** analog of muramyl dipeptide
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(comparison compd.; synthesis of muramyl dipeptide analog-glucomannan **conjugate** and stimulation activity against macrophage-like cells)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

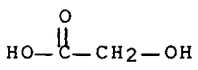
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



IT **9064-52-2DP**, Carboxymethyl Glucomannan, **conjugates** with **glucose** analog of muramyl dipeptide **146916-65-6DP**, conjugates with CM glucomannan
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of muramyl dipeptide analog-glucomannan **conjugate** and stimulation activity against macrophage-like cells)
RN 9064-52-2 HCAPLUS
CN D-Gluco-D-mannan, carboxymethyl ether (9CI) (CA INDEX NAME)

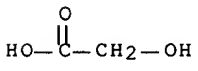
CM 1

CRN 11078-31-2
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3

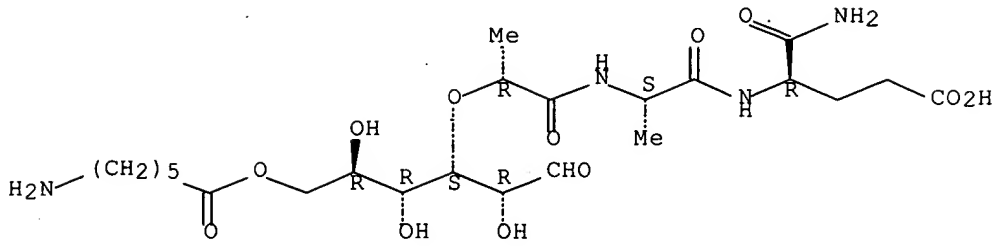


RN 146916-65-6 HCAPLUS
CN D-.alpha.-Glutamine, N2-[N-[2-[6-O-(6-amino-1-oxohexyl)-D-glucos-3-O-yl]-1-oxopropyl]-L-alanyl]-, (R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

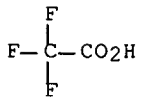
CRN 146916-64-5
CMF C23 H40 N4 O12

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L47 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:549521 HCAPLUS
DOCUMENT NUMBER: 122:312947
TITLE: Method of activating soluble carbohydrate using novel cyanylating reagents for the production of immunogenic constructs
INVENTOR(S): Lees, Andrew
PATENT ASSIGNEE(S): Henry M. Jackson Foundation for the Advancement of Military Medicine, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9508348	A1	19950330	WO 1994-US10658	19940921
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2171942	AA	19950330	CA 1994-2171942	19940921
AU 9478391	A1	19950410	AU 1994-78391	19940921
AU 678613	B2	19970605		
EP 720485	A1	19960710	EP 1994-929273	19940921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09502978	T2	19970325	JP 1994-509897	19940921

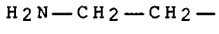
PRIORITY APPLN. INFO.: US 1993-124491 A 19930922
WO 1994-US10658 W 19940921

AB A process for producing an immunogenic construct comprising activating at

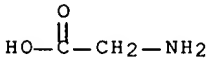
least one first carbohydrate-contg. moiety with a novel cyanylating reagent and covalently joining said activated first moiety to a second moiety. Immunogenic constructs may be prepd. by this process using either direct **conjugation** of first and second moieties or using indirect **conjugation** with a bifunctional reagent. The first carbohydrate is dextran, Pneumococcal **polysaccharide**, Haemophilus influenzae **polysaccharide**, or a viral or bacterial **polysaccharide**; the second carbohydrate is albumin, pertussis toxoid, tetanus toxoid, malaria-derived peptide p28, antibody, toxoid or toxin; the cyanylating reagent is CDAP, CTEA, and pNPC; and the bifunctional reagent is ethylenediamine, 1,6-hexane diamine, adipic dihydrazide, cystamine, glycine, or lysine. In example, **conjugates** of pertussis toxoid and Pneumococcal type 14 **polysaccharide** or Haemophilus influenzae **polysaccharide**, tetanus toxoid and malaria-derived peptide 28, and monoclonal antibody H.delta.a/1 and aminoethyl **carboxymethyl dextran** were prepd. as vaccines.

IT **51-85-4**, Cystamine **56-40-6**, Glycine, biological studies **56-87-1**, L-Lysine, biological studies **107-15-3**, 1,2-Ethanediamine, biological studies **124-09-4**, 1,6-Hexanediamine, biological studies **1071-93-8**, Adipic dihydrazide
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(bifunctional agent; prepn. of immunogenic carbohydrate constructs with cyanylating and bifunctional reagent as vaccine)

RN 51-85-4 HCAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

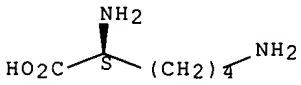


RN 56-40-6 HCAPLUS
CN Glycine (8CI, 9CI) (CA INDEX NAME)

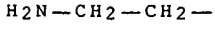


RN 56-87-1 HCAPLUS
CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

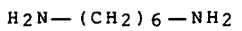


RN 107-15-3 HCAPLUS
CN 1,2-Ethanediamine (9CI) (CA INDEX NAME)

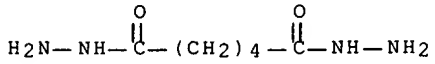


RN 124-09-4 HCAPLUS

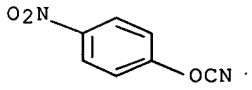
CN 1,6-Hexanediamine (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 1071-93-8 HCAPLUS
CN Hexanedioic acid, dihydrazide (9CI) (CA INDEX NAME)



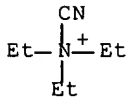
IT **1129-38-0**, p-Nitrophenylcyanate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cyanylating agent; prepn. of immunogenic carbohydrate constructs with cyanylating and bifunctional reagent as vaccine)
RN 1129-38-0 HCAPLUS
CN Cyanic acid, 4-nitrophenyl ester (9CI) (CA INDEX NAME)



IT **30684-36-7 59016-56-7**, 1-Cyano-4-(dimethylamino)-pyridinium tetrafluoroborate
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); USES (Uses)
(cyanylating agent; prepn. of immunogenic carbohydrate constructs with cyanylating and bifunctional reagent as vaccine)
RN 30684-36-7 HCAPLUS
CN Ethanaminium, N-cyano-N,N-diethyl-, tetrafluoroborate(1-) (9CI) (CA INDEX NAME)

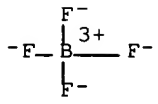
CM 1

CRN 44795-37-1
CMF C7 H15 N2



CM 2

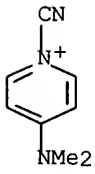
CRN 14874-70-5
CMF B F4
CCI CCS



RN 59016-56-7 HCAPLUS
CN Pyridinium, 1-cyano-4-(dimethylamino)-, tetrafluoroborate(1-) (9CI) (CA INDEX NAME)

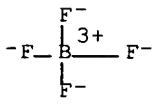
CM 1

CRN 59016-55-6
CMF C8 H10 N3



CM 2

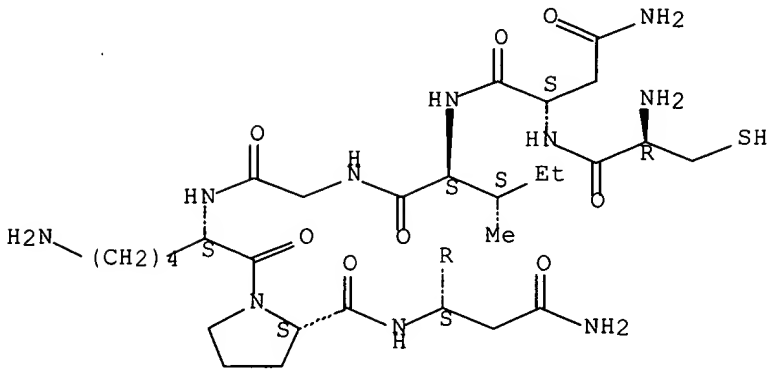
CRN 14874-70-5
CMF B F4
CCI CCS



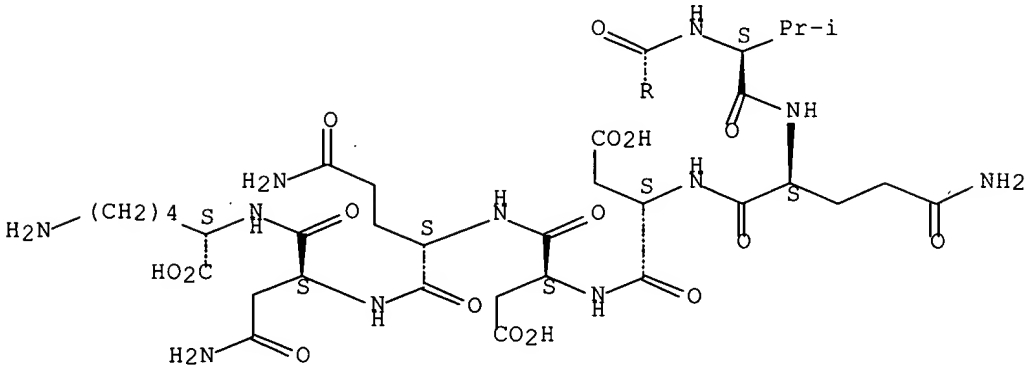
IT **163038-69-5DP**, conjugates with monoclonal antibody
163438-78-6DP, conjugates with monoclonal antibody
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of immunogenic carbohydrate constructs with cyanylating and bifunctional reagent as vaccine)
RN 163038-69-5 HCAPLUS
CN L-Lysine, L-cysteinyl-L-asparaginyl-L-isoleucylglycyl-L-lysyl-L-prolyl-L-asparaginyl-L-valyl-L-glutaminyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-glutaminyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



RN 163438-78-6 HCAPLUS
CN Dextran, 2-aminoethyl carboxymethyl ether (9CI) (CA INDEX NAME)

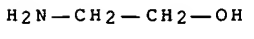
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

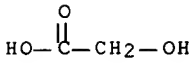
CM 2

CRN 141-43-5
CMF C2 H7 N O



CM 3

CRN 79-14-1
CMF C2 H4 O3



IT **9004-54-0D**, Dextran, conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of immunogenic carbohydrate constructs with cyanylating and bifunctional reagent as vaccine)
RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

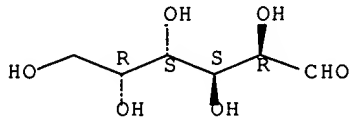
L47 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:289400 HCAPLUS
DOCUMENT NUMBER: 120:289400
TITLE: Manipulation of renal disposition of human recombinant superoxide dismutase by chemical modification
AUTHOR(S): Mihara, Kiyoshi; Sawai, Kenzo; Takakura, Yoshinobu; Hashida, Mitsuru
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: Biol. Pharm. Bull. (1994), 17(2), 296-301
CODEN: BPBLEO; ISSN: 0918-6158
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The renal disposition characteristics of superoxide dismutase (SOD) and its derivs., including macromol. **conjugates** with **polyethylene** glycol and **carboxymethyl-dextran**, cationized deriv., and glycosylated derivs. with **galactose** and mannose, were studied in the isolated perfused rat kidney. Renal disposition processes, such as glomerular filtration, tubular reabsorption, and uptake from the capillary side, were quant. detd. by single-pass indicator diln. expts. under filtering and nonfiltering kidney conditions. Native SOD had a high glomerular filtration rate (40% of that of inulin) and was effectively reabsorbed in the tubules, while no significant uptake was obsd. from capillary side. Macromol. **conjugates** showed restricted glomerular filtration due to an increase in mol. size. Cationization of SOD greatly enhanced its assocn. with the tissue, not only from the luminal side but also from the capillary side, based upon electrostatic interaction. Galactosylated and mannosylated SOD showed reduced tubular reabsorption and increased exposure of the luminal surface to the enzyme. In addn., a small but significant uptake of mannosylated SOD from the capillary side was obsd. This uptake was dose-dependent and completely inhibited by mannan, suggesting that mannose receptor-mediated endocytosis existed in the capillary side of the kidney. Thus, the authors can manipulate the renal disposition profiles of SOD by changing its physicochem. or biol. properties through chem. modification.
IT **9054-89-1**, Superoxide dismutase
RL: BIOL (Biological study)
(human recombinant, kidney disposition of, chem. modification manipulation of)
RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **59-23-4DP**, **Galactose**, **conjugates** with superoxide dismutase **79-14-1DP**, Glycolic acid, conjugates with

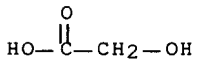
superoxide dismutase **3458-28-4DP**, Mannose, conjugates with superoxide dismutase **9044-05-7DP**, Carboxymethyldextran, conjugates with superoxide dismutase **25322-68-3DP**, **Polyethylene** glycol, conjugates with superoxide dismutase
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and kidney disposition of)

RN 59-23-4 HCAPLUS
CN D-Galactose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

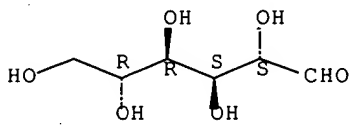


RN 79-14-1 HCAPLUS
CN Acetic acid, hydroxy- (9CI) (CA INDEX NAME)



RN 3458-28-4 HCAPLUS
CN D-Mannose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

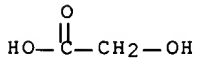
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

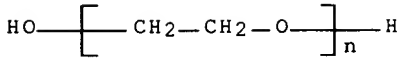
CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX

NAME)



L47 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:235367 HCAPLUS
DOCUMENT NUMBER: 120:235367
TITLE: Control of the disposition profiles of proteins in the kidney via chemical modification
AUTHOR(S): Takakura, Yoshinobu; Mihara, Kiyoshi; Hashida, Mitsuru
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: J. Controlled Release (1994), 28(1-3), 111-19
CODEN: JCREEC; ISSN: 0168-3659
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To construct the strategy to control the renal disposition profiles of protein drugs by chem. modification studies were performed using the perfused rat kidney. Renal disposition processes, i.e., glomerular filtration, tubular reabsorption, and uptake from the vascular side, were quant. detd. by single-pass indicator diln. expts. under filtering and non-filtering conditions. As the first step, the renal disposition characteristics of model protein drugs and macromols. were evaluated. These studies clarified the relationship between physicochem. properties of macromols., such as mol. wt. and elec. charge, and their fate in the kidney in a quant. manner. Based on these findings, an antioxidant enzyme, superoxide dismutase (SOD), selected as a therapeutic agent for various tissue injuries including renal failure mediated by reactive oxygen species, was chem. modified. **Conjugation** with macromols., **polyethylene** glycol and **carboxymethyl dextran**, decreased glomerular filtration of SOD. Cationization enabled the enzyme to distribute to the kidney from the capillary side and to be completely reabsorbed by the tubular epithelium after glomerular filtration based on electrostatic interaction. On the other hand, glycosylation with monosaccharides, **galactose** and mannose, significantly reduced its tubular reabsorption and enhanced its exposure to the luminal surface. Furthermore, the mannosylated deriv. accumulated in the kidney from the vascular side via a mannose-recognition mechanism. Thus, the present study demonstrates that chem. modification is useful for the control of renal disposition characteristics of protein drugs.

IT **9044-05-7D, Carboxymethyl dextran, conjugates** with superoxide dismutase **9054-89-1D**, Superoxide dismutase, conjugates with macromols. **25322-68-3D**, **Polyethylene** glycol, conjugates with superoxide dismutase
RL: BIOL (Biological study)
(disposition profiles of, in kidney)

RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

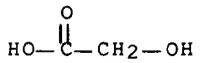
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

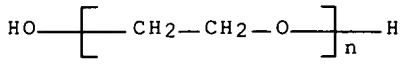
CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



L47 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:226756 HCAPLUS
DOCUMENT NUMBER: 120:226756
TITLE: Targeting delivery of protein drugs by chemical modification
AUTHOR(S): Hashida, Mitsuru; Nishikawa, Makiya; Yamashita, Fumiyoshi; Takakura, Yoshinobu
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: Drug Dev. Ind. Pharm. (1994), 20(4), 581-90
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vivo disposition profiles of protein derivs. having various chem. modifications were systematically compared in mice based on the clearance concept. Proteins such as bovine .gamma.-globulin (IgG), bovine serum albumin (BSA), superoxide dismutase (SOD), soybean trypsin inhibitor (STI), and chicken egg white lysozyme (LZM) were (1) **conjugated** and **polyethylene** glycol (**PEG**) and dextran to increase mol. size, (2) **conjugated** with **carboxymethyl-dextran** (**CMD**) and diethylaminoethyl-dextran (DEAED) or coupled with diaminohexane or succinic acid to introduce elec. charges, and (3) modified with **galactose** (Gal) and mannose (Man) moieties to bestow an affinity for receptor-mediated endocytosis in cells. By applying these modifications, in vivo disposition features of proteins were extensively changed; i.e., in the case of SOD, **conjugation** with **CMD** and **PEG** prolonged its circulation half-life more than 100 times but cationized SOD showed remarkable accumulation on the surface of the liver tissue. In addn., specific targeting to the parenchymal cells of the liver was demonstrated in Gal-SOD, while, Man-SOD and succinylated SOD showed rapid uptake by the nonparenchymal cells. These results revealed the utility of chem. modification for controlling in vivo disposition of proteins.

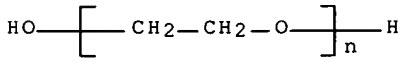
IT **9001-63-2**, Lysozyme **9054-89-1**, Superoxide dismutase **9078-38-0**, Soybean trypsin inhibitor
RL: PROC (Process)
(chem. modification of, for targeting delivery)

RN 9001-63-2 HCAPLUS
CN Lysozyme (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

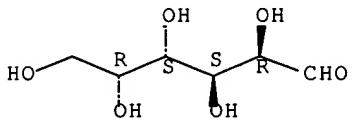
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9078-38-0 HCAPLUS
CN Trypsin inhibitor, soybean (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **25322-68-3, Polyethylene** glycol
RL: BIOL (Biological study)
(protein drugs modified by, for targeting delivery)
RN 25322-68-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)

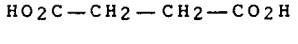


IT **59-23-4**, Galactose, reactions **110-15-6**, Succinic acid, reactions **124-09-4**, Diaminohexane, reactions **3458-28-4**, D-Mannose **9004-54-0**, Dextran, reactions **9015-73-0**, Diethylaminoethyl-dextran **9044-05-7**, Carboxymethyl-dextran
RL: RCT (Reactant)
(protein drugs modified by, for targeting delivery)
RN 59-23-4 HCAPLUS
CN D-Galactose (9CI) (CA INDEX NAME)

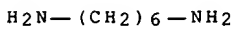
Absolute stereochemistry. Rotation (+).



RN 110-15-6 HCAPLUS
CN Butanedioic acid (9CI) (CA INDEX NAME)

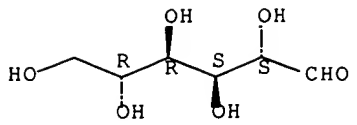


RN 124-09-4 HCAPLUS
CN 1,6-Hexanediamine (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 3458-28-4 HCAPLUS
CN D-Mannose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RN 9015-73-0 HCAPLUS
CN Dextran, 2-(diethylamino)ethyl ether (9CI) (CA INDEX NAME)

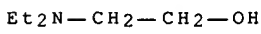
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 100-37-8
CMF C6 H15 N O



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

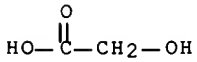
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



L47 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:186083 HCAPLUS
DOCUMENT NUMBER: 120:186083
TITLE: Functional changes of lysozyme by **conjugating** with **carboxymethyl dextran**
AUTHOR(S): Hattori, Makoto; Imamura, Shigeo; Nagasawa, Koichi;

Takahashi, Koji
CORPORATE SOURCE: Fac. Agric., Tokyo Univ. Agric. Technol., Tokyo, 183, Japan
SOURCE: Biosci., Biotechnol., Biochem. (1994), 58(1), 174-7
CODEN: BBBIEJ; ISSN: 0916-8451
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hen egg lysozyme-**carboxymethyl dextran** (HEL-**CMD**) **conjugate** was prepd. by using water-sol. carbodiimide as a model protein-acidic **polysaccharide conjugate** for improving the protein function. An acid-amide bond between HEL and **CMD** was confirmed by SDS-PAGE, isoelec. focusing and IR spectra. The molar ratio of **CMD** to HEL in the **conjugate** was 1:1. The isoelec. point of the **conjugate** was 5.5-6.0, which is much lower than that of HEL. Spectroscopic studies suggested that the conformation around the Trp residue had not changed but the .alpha.-helix content had decreased to about 1/3 that for native HEL. The **conjugate** maintained about 60% of the enzymic activity of native HEL at 40-60 .degree.C, while it was about 1.4 times as active as native HEL at 4 .degree.C and 80 .degree.C. The **conjugate** was more stable to proteolysis than native HEL. The denaturation temp. of the **conjugate** was about 73 .degree.C, which is almost the same as that of native HEL. However, the enthalpy for denaturation of the **conjugate** was about 1/3 that of native HEL, which corresponds to the decrease in .alpha.-helix content.

IT **9001-63-2D**, Lysozyme, **conjugates** with **carboxymethyl dextran 9044-05-7D**, **Carboxymethyl dextran, conjugates** with lysozyme
RL: BIOL (Biological study)
(conformation and thermal stability and catalytic properties of)

RN 9001-63-2 HCAPLUS
CN Lysozyme (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

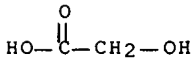
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



L47 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:678527 HCAPLUS
DOCUMENT NUMBER: 119:278527

TITLE: Synthesis and pharmacokinetics of a new liver-specific carrier, glycosylated carboxymethyl-dextran, and its application to drug targeting
AUTHOR(S): Nishikawa, Makiya; Kamijo, Akiko; Fujita, Takuya; Takakura, Yoshinobu; Sezaki, Hitoshi; Hashida, Mitsuru
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: Pharm. Res. (1993), 10(9), 1253-61
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To develop a new carrier system for hepatic targeting, **carboxymethyl-dextran** (**CMD**) was modified with **galactose** and mannose residues (Gal-**CMD**, Man-**CMD**), and their disposition characteristics were studied in mice using 14C-labeled dextran. At a dose of 1 mg/kg, i.v.-injected Gal-**CMD** and Man-**CMD** rapidly accumulated in the liver parenchymal and nonparenchymal cells, resp., because of their preferential uptake via carboxylate receptors in these cells. Pharmacokinetic anal. revealed that their uptake rates were sufficiently large for selective drug targeting. Targeting of cytosine .beta.-D-arabinoside (araC) was studied using Gal-**CMD** as a sp. carrier to the hepatocytes. From the **conjugate** of araC with Gal-**CMD**, araC was released with a half-life of 36 h in phosphate buffer (pH 7.4) and 23 h in plasma. An in vivo biodistribution study demonstrated a disposition profile of the **conjugated** araC similar to that of the carrier, and selective delivery to hepatocytes of up to 80% of the dose was achieved. These findings suggest that glycosylated **CMDs** are carriers with a high affinity to liver parenchymal and nonparenchymal cells without any affinity to other tissues.

IT **9044-05-7**, Carboxymethyl dextran
RL: RCT (Reactant)
(glycosylation of, for drug targeting to liver)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

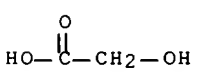
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3

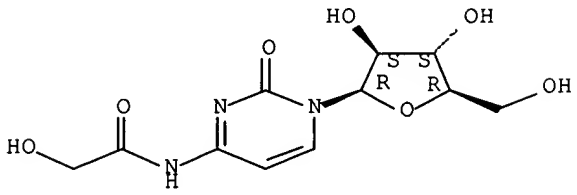


IT **151615-76-8P 151615-77-9P 151615-78-0P 151615-79-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and pharmacokinetics of, for drug targeting to liver)
RN 151615-76-8 HCAPLUS
CN Dextran, 2-[(1-.beta.-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]-2-oxoethyl carboxymethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 171340-32-2
CMF C11 H15 N3 O7
CDES 5:B-D-ARABINO

Absolute stereochemistry.



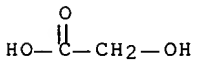
CM 2

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 3

CRN 79-14-1
CMF C2 H4 O3

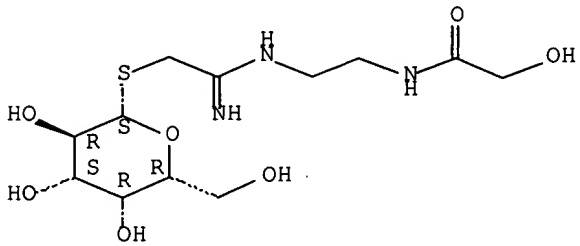


RN 151615-77-9 HCAPLUS
CN Dextran, 2-[(1-.beta.-D-arabinofuranosyl-1,2-dihydro-2-oxo-4-pyrimidinyl)amino]-2-oxoethyl carboxymethyl 2-[[2-[[2-(.beta.-D-galactopyranosylthio)-1-iminoethyl]amino]ethyl]amino]-2-oxoethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 171340-34-4
CMF C12 H23 N3 O7 S
CDES 5:B-D-GALACTO

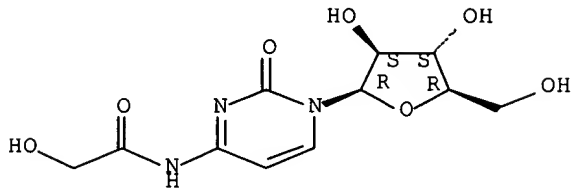
Absolute stereochemistry.



CM 2

CRN 171340-32-2
CMF C11 H15 N3 O7
CDES 5:B-D-ARABINO

Absolute stereochemistry.



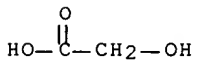
CM 3

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 4

CRN 79-14-1
CMF C2 H4 O3

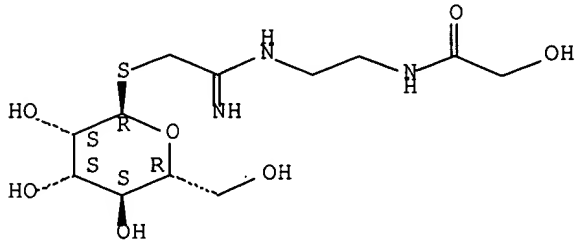


RN 151615-78-0 HCAPLUS
CN Dextran, carboxymethyl 2-[[2-[[1-imino-2-(.alpha.-D-mannopyranosylthio)ethyl]amino]ethyl]amino]-2-oxoethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 171340-33-3
CMF C12 H23 N3 O7 S
CDES 5:A-D-MANNO

Absolute stereochemistry.



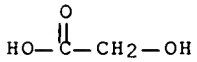
CM 2

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 3

CRN 79-14-1
CMF C2 H4 O3

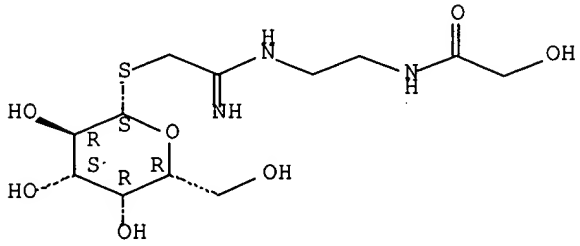


RN 151615-79-1 HCAPLUS
CN Dextran, carboxymethyl 2-[[2-[[2-(.beta.-D-galactopyranosylthio)-1-iminoethyl]amino]ethyl]amino]-2-oxoethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 171340-34-4
CMF C12 H23 N3 O7 S
CDES 5:B-D-GALACTO

Absolute stereochemistry.



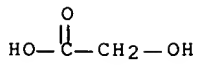
CM 2

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

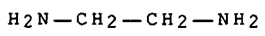
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 3

CRN 79-14-1
CMF C2 H4 O3

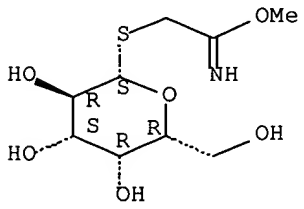


IT **107-15-3**, 1,2-Ethanediamine, reactions
RL: RCT (Reactant)
(reaction of, with carboxymethyl dextran)
RN 107-15-3 HCAPLUS
CN 1,2-Ethanediamine (9CI) (CA INDEX NAME)



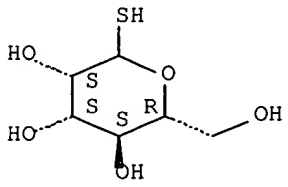
IT **75204-21-6 151530-12-0**
RL: RCT (Reactant)
(reaction of, with carboxymethyl dextran ethylenediamine deriv.)
RN 75204-21-6 HCAPLUS
CN Ethanimidic acid, 2-(.beta.-D-galactopyranosylthio)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



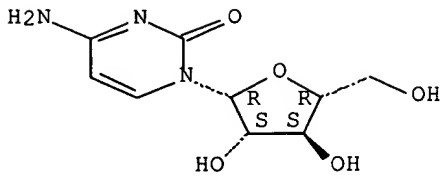
RN 151530-12-0 HCAPLUS
CN D-Mannopyranose, 1-thio- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **147-94-4**, Ara-C
RL: BIOL (Biological study)
(targeting of, to liver, glycosylated carboxymethyl dextran deriv. for)
RN 147-94-4 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-.beta.-D-arabinofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



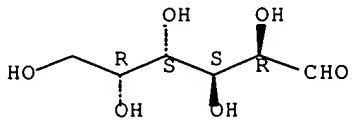
L47 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:116685 HCAPLUS
DOCUMENT NUMBER: 118:116685
TITLE: Therapeutic effects of superoxide dismutase derivatives modified with mono- or polysaccharides on hepatic injury induced by ischemia/reperfusion
AUTHOR(S): Fujita, Takuya; Furitsu, Hisao; Nishikawa, Mikiya; Takakura, Yoshinobu; Sezaki, Hitoshi; Hashida, Mitsuru
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: Biochem. Biophys. Res. Commun. (1992), 189(1), 191-6
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Therapeutic effects of four types of recombinant superoxide dismutase (SOD) derivs., **conjugates** with polysaccharides, carboxymethyl (SOD-**CMD**) and diethylaminoethyl (SOD-DEAED) dextrans and galactosylated (Gal-SOD) and mannosylated (Man-SOD) derivs., on hepatic ischemia/reperfusion injury were studied in rats. Hepatic injury induced by transient occlusion and subsequent reflow of hepatic blood was evaluated by the anal. of biliary excretion of bromosulfophthalein (BSP) injected i.v. At a dose of 1000 units/kg, native SOD and SOD-DEAE had no significant effect and SOD-**CMD** had a slight effect. On the other hand, Gal-SOD an Man-SOD, targeted to liver parenchymal and nonparenchymal cells, resp., by a receptor-mediated endocytosis, exhibited superior inhibitory effects. These results demonstrated that these glycosylated SOD derivs. were useful for the prevention of hepatic ischemia/reperfusion injury.

IT **59-23-4D**, D-**Galactose**, superoxide dismutase **conjugates** **3458-28-4D**, D-Mannose, superoxide dismutase conjugates **9015-73-0D**, Diethylaminoethyl dextran, superoxide dismutase conjugates **9044-05-7D**, Carboxymethyldextran, superoxide dismutase conjugates **9054-89-1D**, Superoxide dismutase, polysaccharide derivs.
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antioxidant activity of, in liver injury from ischemia/reperfusion)

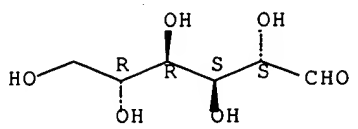
RN 59-23-4 HCAPLUS
CN D-Galactose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 3458-28-4 HCAPLUS
CN D-Mannose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 9015-73-0 HCAPLUS
CN Dextran, 2-(diethylamino)ethyl ether (9CI) (CA INDEX NAME)

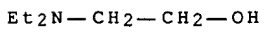
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 100-37-8
CMF C6 H15 N O



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

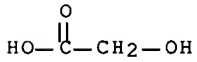
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L47 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:66727 HCAPLUS
DOCUMENT NUMBER: 118:66727
TITLE: Targeted delivery of human recombinant superoxide dismutase by chemical modification with mono- and

polysaccharide derivatives
AUTHOR(S): Fujita, Takuya; Nishikawa, Makiya; Tamaki, Chieko; Takakura, Yoshinobu; Hashida, Mitsuru; Sezaki, Hitoshi
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606-01, Japan
SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(3), 971-8
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

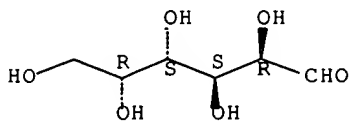
AB Four types of superoxide dismutase (SOD) derivs. such as SOD-**carboxymethyl dextran conjugate**, SOD-diethylaminoethyl dextran **conjugate**, galactosylated SOD and mannosylated SOD were synthesized and their potential for selective targeting to organs or cells was evaluated in mice by pharmacokinetic anal. All SOD derivs. retained 50 to 80% for 3 h. After i.v. injection, native SOD was rapidly excreted into urine and no significant accumulation was obsd. in the organs except the kidney. SOD-**carboxymethyl dextran conjugate** gave a long plasma half-life because of impaired glomerular filtration and tissue interaction. By contrast, galactosylated SOD and mannosylated SOD were very rapidly eliminated from the circulation and taken up by parenchymal and nonparenchymal cells of the liver, resp., via receptor-mediated endocytosis. These uptake processes were nonlinear and hepatic uptake clearance decreased as the dose increased, although almost complete extn. was obtained at a dose of 0.1 mg/kg. Furthermore, the accumulation in kidney of both glycosylated SODs was drastically decreased due to reduced renal proximal tubular reabsorption and also enhanced hepatic clearance. SOD-diethylaminoethyl dextran **conjugate** also rapidly disappeared from plasma and distributed into liver, but its accumulation occurred due to electrostatic interaction and was nonspecific in cellular distribution. These results suggest the possibility of controlling the in vivo fate of SOD at a cellular level by chem. modification utilizing sugar moieties with varied physicochem. and/or biol. characteristics.

IT **9054-89-1**, Superoxide dismutase
RL: BIOL (Biological study)
(human recombinant, targeted delivery of, by chem. modification with polysaccharides)
RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

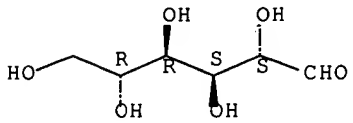
IT **59-23-4DP, Galactose, conjugates** with superoxide dismutase **3458-28-4DP**, Mannose, conjugates with superoxide dismutase **9015-73-0DP**, Diethylaminoethyl dextran, conjugates with superoxide dismutase **9044-05-7DP**, **Carboxymethyl dextran, conjugates** with superoxide dismutase **9054-89-1DP**, Superoxide dismutase, conjugates with polysaccharides
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for targeted drug delivery)
RN 59-23-4 HCAPLUS
CN D-Galactose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 3458-28-4 HCAPLUS
CN D-Mannose (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 9015-73-0 HCAPLUS
CN Dextran, 2-(diethylamino)ethyl ether (9CI) (CA INDEX NAME)

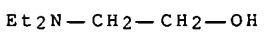
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 100-37-8
CMF C6 H15 N O



RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

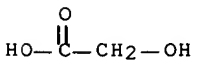
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9054-89-1 HCAPLUS
CN Dismutase, superoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L47 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:571374 HCAPLUS

DOCUMENT NUMBER: 103:171374
TITLE: Carbohydrate-containing derivatives of the trypsin-kallikrein inhibitor aprotinin from bovine organs. II. Inhibitor coupled to the (carboxymethyl)dextran derivatives of D-galactose
AUTHOR(S): Larionova, N. I.; Mityushina, G. V.; Kazanskaya, N. F.; Blidchenko, Yu. A.; Berezin, I. V.
CORPORATE SOURCE: Dep. Chem., M. V. Lomonosov Moscow State Univ., Moscow, 119899, USSR
SOURCE: Biol. Chem. Hoppe-Seyler (1985), 366(8), 743-8
CODEN: BCHSEI
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The trypsin-kallikrein inhibitor aprotinin was coupled to 2 (**carboxymethyl)dextran** derivs. of D-**galactose**; the **conjugates** contained 14 and 38 D-**galactose** residues/mol of protein, resp. The apparent dissocn. consts. Ki of the complexes between trypsin and modified aprotinins proved to be one order of magnitude higher than the resp. values for native aprotinin. The distribution of the modified aprotinins in rat organs after endocardial injection was studied. The **conjugates** of aprotinin with (**carboxymethyl)dextran** derivs. of D-**galactose** were characterized by decreased clearance rates; they accumulated in the active form in liver. The accumulation was 2.5-10 times higher than native aprotinin for the time of observation (5 min-2 h).

IT **9044-05-7DP**, galactose derivs., aprotinin complexes
9087-70-1DP, complexes with (carboxymethyl)dextran galactose derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and pharmacokinetics of)

RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

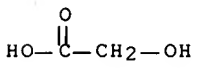
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 9087-70-1 HCAPLUS
CN Trypsin inhibitor, pancreatic basic (9CI) (CA INDEX NAME)

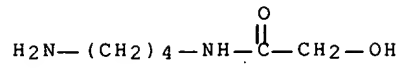
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **98913-51-0DP**, reaction products with lactose
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with lactose)

RN 98913-51-0 HCAPLUS
CN Dextran, 2-[(4-aminobutyl)amino]-2-oxoethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 171263-10-8
CMF C6 H14 N2 O2



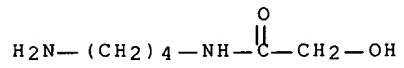
CM 2

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **98913-51-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 98913-51-0 HCAPLUS
CN Dextran, 2-[(4-aminobutyl)amino]-2-oxoethyl ether (9CI) (CA INDEX NAME)

CM 1

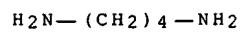
CRN 171263-10-8
CMF C6 H14 N2 O2



CM 2

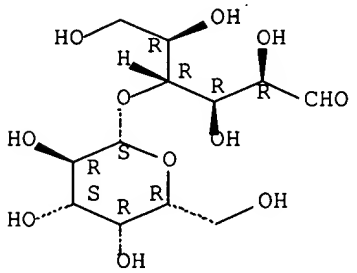
CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **110-60-1**
RL: RCT (Reactant)
(reaction of, with (carboxymethyl)dextran and carbodiimide)
RN 110-60-1 HCAPLUS
CN 1,4-Butanediamine (8CI, 9CI) (CA INDEX NAME)



IT **63-42-3**
RL: RCT (Reactant)
(reaction of, with butylamino(carboxymethyl)dextran)
RN 63-42-3 HCAPLUS
CN D-Glucose, 4-O-.beta.-D-galactopyranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **9044-05-7**
RL: RCT (Reactant)
(reaction of, with diaminobutane and carbodiimide)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

CM 2

CRN 79-14-1
CMF C2 H4 O3